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B. Influenza	100	B. Influenza	250	B. Influenza	500
Diph heroid (Oral)	25	Diph heroid (Oral)	50	Diphtheroid (Oral)	100
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(Curative)

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Pneumobacillus	10	Pneumobacillus	25	Pneumobacillus	50
Micro Catarrhalis	50	Micro Catarrhalis	100	Micro Catarrhalis	200
B. Influenza	100	B. Influenza	250	B. Influenza	500
Diphtheroid (Oral)	10	Diph heroid (Oral)	25	Diphtheroid (Oral)	50
Staphylococcus	50	Staphylococcus	150	Staphylococcus	250
Streptococcus	10	Streptococcus	25	Streptococcus	50

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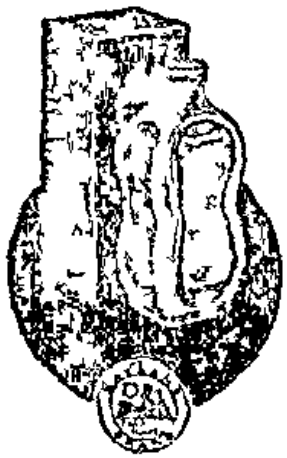
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The Prescriber.

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OUR THIRTIETH VOLUME.

With the present issue The Prescriber begins its thirtieth volume, and though the corresponding birthday will not occur until October, it may not be inappropriate to mention the matter now. Readers of this journal, especially those who have been readers since its inception in 1906, may be interested in being reminded of its age. The time for trumpet blowing is not yet, but the Editor may be pardoned if he indulges for the moment in a retrospective glance.

The period of this journal's existence has been marked by some of the greatest discoveries of medical science. Between 1906 and 1936 each decade has had its own particular triumph: salvarsan in 1910, insulin in 1922, liver therapy in 1927. These events alone mark the period as one of great advance. In 1906 endocrinology as a science simply did not exist: it is true that something was known about the thyroid gland and that adrenaline had been isolated, but it was not until 1907 that Starling demonstrated the chemical co-ordination of the activities of the body and disclosed the existence of hormones. The first special number on this subject in any country was published by The Prescriber in 1913. Since then the science of endocrinology has advanced with great strides and to-day it occupies a foremost position in medical science.

These are but a few of the many advances that have taken place during the past three decades—they are offered merely as an indication of the progress made during that time. With this indication, and in the confident hope of continued advance, The Prescriber starts its thirtieth volume by wishing its readers the world over a

Happy and Prosperous New Year.

ANNUS THERAPEUTICUS:

A Review of Treatment during 1935.

THE beginning of a new year affords a suitable opportunity to review the progress of therapeutics during the twelve months just concluded While nothing very remarkable has happened, there is evidence of steady progress in all departments —progress which is cumulative in its effect, for an innovation may require years for its development and each year registers a definite step forward

The following pages present a brief summary of the work done during 1935 in regard to the treatment of disease Brevity is a necessary feature in such a review, but an effort has been made to include every important development having a practical bearing on therapeutics Many of the subjects will be treated at greater length in the regular Abstract Reviews appearing during succeeding months; meanwhile a list of references is given at the end of each section to enable readers, should they so desire, to get fuller details from the original To save space, certain journals whose titles are lengthy and which are referred to with frequency are designated by initials: these are given below, other contractions being self-explanatory.

Am J.M.Sc —American Journal of the Medical Sciences (Philadelphia)
Am J O G —American Journal of Obstetrics & Gynecology (St Louis)
Arch D &S —Archives of Dermatology & Syphilology (Chicago)
B J D &S —British Jour of Dermatology & Syphilis (London)
B J V D —British Journal of Venereal Diseases (London)
B M J —British Medical Journal (London)
C M.A J —Canadian Medical Association Journal (Montreal)
D m W —Deutsche medizinische Wochenschrift (Leipzig)
I J.M R —Indian Journal of Medical Research (Calcutta)
I.M G —Indian Medical Gazette (Calcutta)
J.A.M A —Journal of the American Medical Association (Chicago)
J.L C.M —Journal of Laboratory and Clinical Medicine (St Louis)
J Ph.Ex Th —Jour of Pharmacology & Exper Therapeutics (Baltimore)
J R A M C —Journal Royal Army Med Corps (London)
M m W —Münchener medizinische Wochenschrift (Munich)
N Eng J M —New England Jour Medicine (Boston)
N Y St J.M —New York State Journal of Medicine (New York)
P R.S.M —Proceedings of the Royal Society of Medicine (London)
Q J M —Quarterly Journal of Medicine (Oxford)
Q J Ph —Quarterly Journal of Pharmacy (London)
S.Af M J —South African Med Jour (Cape Town)
S m W —Schweizerische medizinische Wochenschrift (Basle)
W k W —Wiener klinische Wochenschrift (Vienna)

When a fuller reference can be found in THE PRESCRIBER, the letter P, followed by month and page, is added in brackets · thus (P June 213) indicates that the subject is more fully treated in THE PRESCRIBER of June 1935, page 213

ANAEMIA.

Research on the anaemias continues and the literature on the subject is still voluminous Efforts at classification are still in evidence, but in the absence of more definite knowledge regarding causation the results are naturally somewhat superficial as knowledge advances the basis of classification tends to change The association of anaemia with certain other conditions, such as hookworm, scurvy, etc, has been studied more closely, and some of these associated anaemias are now regarded as clinical entities

The nutritional anaemia of infancy and childhood has been the subject of much useful work The value of iron therapy in this and in certain other forms of anaemia is now established, and the part played by copper and other catalysts is being studied more closely

Work on pernicious anaemia has been directed largely towards the discovery of the active agent in liver extracts and in desiccated stomach, and certain progress has been reported Work has also been done on subacute combined degeneration of the spinal cord and its prevention and treatment

Considerable attention has been paid to a recently recognized disease of the blood—agranulocytic angina or agranulocytosis and its treatment, while the part played in its causation by certain drugs, such as amidopyrine and barbiturates, has been further investigated A useful brochure on the subject (Report No 76) has been issued by the Ministry of Health

A very full survey of the work done during 1934 appeared in our issue of February 1935, and another, reviewing the work of 1935, will appear in these pages next month

General —Survey to date —PRESCR, Feb '35, pp 49 70

Some recent advances in the treatment of the anaemias (J D Comrie) —PRESCR, Feb '35, p 41

Several articles diagnosis, treatment, etc —*Practr*, Mar '35, p 249 *et seq*

Blood diseases seven articles —*D m W*, Sept 27, '35, pp 1543-1558

Classification and differential diagnosis of the anaemias (R L Haden) —*J A M A*, Mar 2, '35, p 706

Differential diagnosis and treatment of severe anaemia (J C Matthews) —*B M J*, Nov 16, 35, p 943

Application of diagnostic criteria to treatment (F H Bethell) —*N Y St J M*, Aug 15, '35 p 799

Amount of haemoglobin in the blood (E R Holiday *et al*) —*Lancet*, Sept 21, '35 p 661

The laboratory as an approach to anaemia therapy (T G Schnabel) —*J L C M*, Apr '35, p 714

Haemoglobin regeneration as influenced by diet, etc (G H Whipple) —*J A M A* Mar 9 '35, p 791

Ultraviolet irradiation for secondary anaemia (Kovacs and Leavy) —*N Y St J M* Aug 15 '35, p 825

Facts concerning treatment (W P Murphy)—*N Y St J M*, Oct 1, '35, p 973

Anaemia in the chronic rheumatic diseases (D H Collins)—*Lancet*, Sept 7, '35, p 548

Effect of ascorbic acid on anaemia of scurvy (Dunlop and Scarborough)—*Edinb M J*, Sept '35, p 476

Achresthic anaemia a group of megalocytic anaemias closely resembling pernicious anaemia (Wilkinson and Israels)—*B M J*, Jan 26; Feb 2, '35, pp 139, 194

The acute haemolytic anaemia of Lederer (Joules and Masterman)—*B M J*, July 27, '35, p 150

A typical megalocytic anaemia (G D Kersley)—*B M J*, Nov 23, '35, p 994

Aplastic anaemia blood transfusion and pentose nucleotide (J McD Holmes)—*Lancet*, July 13, '35, p 71

Aplastic anaemia following neoarsphenamine (A H Imrie)—*Lancet*, July 13, '35, p 73

Macrocytic anaemia with aplastic features following application of hair dye (C W Baldridge)—*Am J M Sc*, June '35, p 759

Splenic anaemia (J McMichael)—*Edinb M J*, June '35 (Med.-Chir. Soc.), p 97

Splenic anaemia ligation of splenic artery (R B Watson)—*B M J*, Apr 20, '35, p 821

Hookworm anaemia massive doses of iron (J C Banerjea)—*Ind J Pediat*, Oct '35, p 314

Anaemia of Infancy.—Anaemia in infancy and childhood (Helen M M Mackay)—*Practr*, Aug '35, p 200

Anaemia in childhood (I Wood)—*M J Australia*, Aug 17, '35, p 211

Anaemias of nutritional deficiency aetiology, diagnosis, treatment, prevention (G R. Minot)—*J A M A*, Oct 12, '35, p 1176

Haemorrhage and anaemia in the new-born (R Lightwood)—*Med Press* Oct 23, '35 (supp.), p xi

Congenital anaemia of the new born (Pasachoff and Wilson)—*Am J O G*, Mar '35 p 415

Nutritional iron deficiency anaemia (L S P Davidson *et al*)—*B M J*, Aug 3 '35, p 195

Prophylaxis of anaemia in infancy with iron and copper (S J Usher *et al*)—*Am J Dis Ch*, Mar '35, p 642

Use of iron and iron catalysts in anaemia of children (H Goldstein)—*Arch Pediat*, Apr '35, p 234

Anaemia of Pregnancy.—Haemoglobin level among London mothers and its bearing on susceptibility to infection (H M M Mackay)—*Lancet*, June 22, '35 p 1431

Hypochromic type 60 cases (F R Irving)—*Am J O G*, June '35, p 850

Pernicious Anaemia—Review of 56 hospital cases (Mills and Herring) *Lancet*, Mar 2 '35 p 488

Lengthening life by modern therapy (P Stocks)—*B M J*, May 18, '35, p 1013

General article (J P McGowan)—*Edinb M J*, June '35, p 293

Glands of stomach and pylorus in relation to pernicious anaemia (E Meulengracht)—*P R S M*, May '35, p 841

Colour reaction of serum in p anaemia (Schmele and Schmid)—*Klin Wschr*, May 11, '35, p 675

Interpretation of reticulocyte reactions (Minot and Castle)—*Lancet*, Aug 10, '35, p 319

Pseudo pernicious anaemia in a case of lead poisoning (G Pellegrini)—*Riforma med*, Apr 20, '35, p 589

Liver-resistant cases (A Piney)—*Med Press*, Oct 30, '35, p 385

Development of liver therapy (Minot and Harvard)—*Lancet*, Feb 16, '35, p 361

A concentrated liver extract for parenteral use (Scowen and Spence)—*B M J*, Feb 9, '35, p 246

Anti anaemic material of liver and stomach (R West)—*J A M A*, Aug 10, '35, p 432

Chemical nature of haematopoietic substance in liver (Dakin and West)—*J Biol Chem*, May '35, p 489

Increased potency of liver extract after incubation with human gastric juice (P J Fouts *et al*)—*Ann Int Med*, Jan '35, p 790

Effect of autolysis on potency of liver (Castle and Strauss)—*J.A.M A*, Mar 9, '35, p 798

Massive intramuscular doses of liver extract (Gardner and Wood)—*M J Australia*, May 4, '35, p 543

Methaemoglobin test for anti anaemic action of liver extracts (Wilkinson and Deutsch)—*Klin Wschr*, June 29, '35, p 926

Congo red in pernicious anaemia (Massa and Zolezzi)—*Klin Wschr*, Feb 16, '35, p 235

Mental changes associated with pernicious anaemia (C W Osgood)—*J.A M.A*, June 15, '35, p 2155

Treatment of subacute combined degeneration (W R Brain)—*B.M J*, Nov 30, '35, p 1056

Subacute combined degeneration of the spinal cord arrest with parenteral liver therapy (M B Strauss *et al*)—*J.A M A*, May 4, '35, p 1587

Subacute combined degeneration importance of rest and liver therapy (R F Farquharson)—*C M.A J*, Nov '35, p 473

Agranulocytosis —Certain aspects of a recently recognized disease of the blood—agranulocytosis or agranulocytic angina (E W Adams)—*Ministry of Health Report*, No 76 (H M Staty Office, 6d)

Case reports (G S Smith, F T Ranson, B J Boulton)—*Lancet*, Mar 16, '35, pp 607, 609, Sept 14, '35 p 610

A case of malignant neutropenia (F S Dorrance)—*C.M A J*, Nov '35, p 530

Report of three cases (M M Suzman)—*S.Af M J*, July 13, '35, p 449

Meningitic symptoms with changes in cerebrospinal fluid (K Goadby *et al*)—*Lancet*, Oct 26, '35, p 933

General article (A S Walker)—*M J Australia*, Aug 3, '35, p 133

Relationship of drug therapy to agranulocytosis (Kracke and Parker)—*J A M.A*, Sept 21, '35, p 960

Experimental studies toxic effects of bacterial products recovered from cases—*J L C.M*, July '35, p 1053

Aetiology relationship of amidopyrine (F Stenn)—*J.L C.M*, Aug '35, p 1150

Amidopyrine, barbiturates, etc, in relation to agranulocytosis (V L Bolton)—*J.L C.M*, Aug '35, p 1199

ANAESTHESIA

By far the greatest number of reports concern the use of evipan, the intravenous barbiturate, the use of which for short operations is gaining ground Experiments are reported which show the possibility of its use in prolonged operations

Cyclopropane, a promising anaesthetic gas, has been the subject of further trials, but the difficulty of obtaining it in sufficient quantity still militates against its general use A recent report describes the trial in 250 cases of a product experimentally produced in this country, with very encouraging results

Basal narcosis is still much in favour, both avertin and the barbiturates being successfully employed A report from Germany describes the use of pernocton orally in the form of tablets The subject of Anaesthesia was fully reviewed in our issue of April 1935, the following being the more important communications appearing since then

Abstract review —PRESCR , Apr '35, pp 103-118

Report by Joint Anaesthetics Committee on newer anaesthetics (C A Hadfield) —*P R S M* , June '35, p 1133

New anaesthetic agents and methods (F B Parsons) —*Practitioner*, Oct '35, p 577

Anaesthesia for tonsillectomy (A P Gorham) —*B M J* , July 20, '35, p 112

Analgesics in labour (J E Stacey) —*B M J* , Apr 20, '35, p 817

General anaesthesia in allergic patients (André and Grove) —*N Y St J M* , May 15, '35, p 522

Pre-operative medication (D S Middleton) —*Edinb M J*, May '35 (Med Chir Soc) p 79

Premedication in general anaesthesia (W I T Hotten) —*M J Australia*, July 6, '35, p 5

An explosion in anaesthetic apparatus (R Ironside) —*P R S M* , June '35, p 1127

Electrical ignition of explosive mixtures (G J Finch) —*P R S M* , June '35, p 1130

Resuscitation with complete recovery following apparent death under anaesthesia (R A Grant) —*B M J*, July 13, '35, p 64

Avertin —As a complete anaesthetic in children (J Boyd) —*B M J* , June 1, '35, p 1120

In thyroid surgery 60 cases (K M Heard) —*C M A J*, Oct '35, p 395

Premedication in operative gynaecology (J L Reycraft) —*Am J O G* , Sept '35, p 332

An unusual dose (H K Ashworth) —*B M J* , Nov 16, '35, p 950

Influence of avertin upon renal function (N E Pitt) —*Lancet*, Mar 30, '35, p 741

Barbiturates —Use in primiparous labours (Tritsch and Brown) —*Am J O G* , May '35, p 700

The use of nembutal in childbirth (W J Rawlings) —*M J Australia*, July 6, '35, p 12

Use of nembutal in obstetrics 205 cases (J P Boylan)—*Am J O G*, Mar '35, p 440

Cyclopropane—Morbidity and mortality compared with other agents (Schmidt and Waters)—*Anes & Analg*, Jan-Feb '35, p 1

Signs of depth in cyclopropane anaesthesia (F T Romberger)—*Anes & Analg*, Mar-Apr '35, p 65

Report based on 250 cases (S Rowbotham *et al*)—*Lancet*, Nov 16, '35, p 1110

Divinyl Oxide—Vinethene a new anaesthetic (E W Dörffel)—*D m W*, June 14, '35, p 955

Ether.—Convulsions (H J King)—*Am J Surg*, Oct, '35, p 182

Evipan-Sodium—In general practice (C M Douglas)—*B M J*, June 15, '35, p 1233

As an intravenous anaesthetic (Jarman and Abel)—*P R S M*, Jan '35, p 341, also *Anes & Analg*, Mar-Apr '35, p 54

Technique of evipan anaesthesia (A Dickson)—*Lancet*, May 4, '35, p 1040

Intravenous anaesthesia with evipan in 100 gynaecological cases (Holman and Mathieu)—*Am J O G*, July '35, p 118

Experience in India (P N Banerjee)—*I M G*, July '35, p 380

For minor surgical operations (H K Wang)—*Chinese M J*, Apr '35, p 357

Record of 100 consecutive cases (A W Woo)—*Chinese M J*, Apr '35, p 352

Experiments with evipan in prolonged anaesthesia (Maloney and Hertz)—*J L C M*, Sept '35, p 1260

Use in ophthalmic surgery (I L Johnstone)—*B M J*, Apr 13, '35, p 761

In eye surgery further experiences (T K Lyle)—*B M J*, Apr 13, '35, p 763 (P Apr 115)

Evipan anaesthesia in urology (Greenberger and Bass)—*Urol & Cut Rev*, Aug '35, p 355

Value of evipan anaesthesia in urology (E L Merritt)—*Urol & Cut Rev*, Oct '35, p 709

Nitrous Oxide—Gas air analgesia for children (R J Minnitt)—*Liverpool Med Chir J*, '35, II, p 120

Miscellaneous—Trichlorethylene anaesthesia (C Striker *et al*)—*Anes & Analg*, Mar-Apr '35, p 68

Rectidon in labour (K Jonas)—*M m W*, May 16, '35, p 787

Pernocton (tablets) orally as basal narcotic (H Siepert)—*D m W*, May 10, '35, p 755

Intravenous anaesthesia with eunarcon (O Doring)—*D m W*, May 31, '35, p 868

ANALGESIA

This term is employed to denote those methods of producing insensibility to pain which do not involve loss of consciousness The literature on this subject during the past year contains little that is new advocates of local and spinal analgesia continue to report favourably on their employment for various operations An

improved formula for local analgesics in oil, having prolonged action and being painless on injection, has been advocated for use in rectal surgery

Abstract review—PRESCR, Apr '35, p 119
Local—Local analgesia in gynaecology (A A Davis)—*B M J* Mar 30, '35, p 636
Some principles of local analgesia (L Adam)—*Surg, Gyn & Obst* Mar '35, p 675
Premedication for local anaesthesia (C E Corlette)—*M J Australia* July 6, '35, p 1
Oil soluble analgesics in rectal surgery (C N Morgan)—*B M J* Nov 16, '35, p 938
Extemporaneous preparation of buffered solution (C H Burmeister)—*J Am Dent Assoc*, Sept '35, p 1514
Sensitization to procaine (L M Mullen)—*C M A J*, Sept '35, p 306
Experiences with pantocain (dercain) (H Florcken)—*M m W* Jan 17, '35, p 92
Spinal—Seven years' experience in private practice (E H Wood)—*C M A J*, Sept '35, p 298
Spinal analgesia general article (Stein and Tovell)—*Am J Surg*, Nov '35, p 282
Percaine 800 spinal analgesias by Howard Jones method (F Trempe)—*C M A J*, Aug '35, p 169
Anuria treated with spinal analgesia (Hayes and Paramore)—*Lancet*, Sept 7, '35, p 554

ANTISEPTICS.

Biochemical investigations of the more important antiseptics continue to be reported, but nothing very startling has been announced Improved formulae for the preparation of acriflavine emulsion have been presented and discussed Mercurial antiseptics are still popular, further work has been done on phenylmercuric nitrate and on mercurochrome A new chlorine compound for dental use, azochloramid, has attracted some attention in America. The subject of antiseptics was reviewed in our issue of June

Abstract review acridine compounds, mercurial antiseptics, trypan-blue, azochloramid—PRESCR, June '35, p 208
Acriflavine emulsion a simple formula (J W Tomb)—PRESCR, June '35, p 207
Acriflavine emulsion (W Trillwood)—PRESCR., Oct '35, p 293
Acriflavine emulsions (E A Lum)—*Pharm J*, Nov 2, '35, p 457
Fungicidal power of phenol derivatives (G J Woodward *et al*)—*J L C M*, June '35, p 950
The hypochlorites as antiseptics (Stacy and Wardlaw)—*M J Australia*, June 1, '35, p 682
Antiseptic action of urea (Foulger and Foshay)—*J L C M*, Aug '35, p 1113
Preparation of sterile solutions (H Davis)—*Q J Ph*, July-Sept '35, p 361

Mercurochrome determination of mercury content (Corran and Rymill)—*Q J.Ph*, July Sept, '35, p 340

Mercurochrome action on skin and in infected wounds (J H Hill)—*J A M.A*, July 13, '35, p 100

Mercurochrome in obstetrics (H W Mayes)—*Am J O G*, July '35, p 80

Phenylmercuric nitrate in gynaecology (L H Biskind)—*Lancet*, Nov 9, '35, p 1049

ASTHMA AND HAY FEVER.

An excellent review of recent work on asthma will be found in the Report of the Asthma Research Council, in which progress is reviewed for the year ended 31st October 1935 The Report is obtainable free of charge from the Secretary at King's College, London, W C 2 A number of general articles on asthma and hay fever have appeared in medical literature, of these the following are the more important

Symposium on asthma 7 papers—*Med Press*, May 15, '35

Hypochlorhydria in asthma (M Gillespie)—*Q J M*, Oct '35, p 397

The treatment of asthma (G W Bray)—*B.M J*, Jan 19, '35, p 119

Ditto (J L Livingstone)—*Practitioner*, May '35, p 591

A criterion for treatment of asthma (Conybeare and Witts)—*Guy's Hosp Rep*, Apr '35

Suggestions regarding treatment in childhood (W D Allan)—*Glasgow M J*, Nov '35, p 225

Value of breathing exercises in asthma (Livingstone and Gillespie)—*Lancet*, Sept 28, '35, p 705

Practical method of dealing with asthma and hay fever (R S Steel)—*M J Australia*, July 27, '35, p 114

Gold salts intravenously (L Bansky)—*Lancet*, July 13, '35, p 79 (P Nov 358)

Apomorphine affords relief (D P Anderson)—*C M A J*, July '35, p 74 (P Sept 287)

Hay fever and its treatment (C Francis)—*Practitioner*, May '35, p 601

Hay fever immunological mechanism, diagnosis, treatment (D Harley)—*B M J*, Apr 13, '35, p 754

Effect of pollen therapy on common cold in hay fever subjects (L Sternberg)—*N Y St J M*, July 15, '35, p 713

CANCER.

A striking announcement was made in October by H C Connell, a Canadian physician, who claims to have treated cancer successfully with a preparation of proteolytic enzymes which he calls 'ensol,' the composition of which has been divulged The announcement has been commented on sympathetically but cautiously by the medical press on both sides of the Atlantic Treatment of cancer by proteolytic enzymes was suggested by an Edinburgh worker thirty years ago, and was discussed at some length in these pages

at the time (PRESCR., Feb. '07, p. 70). The uses of radium have again been reported on by the Medical Research Council, and this was reviewed in our issue of December. Beyond these, little of importance has appeared, though the usual sensational reports continue to appear in the daily press. The work of the British Empire Cancer Campaign, as described in its twelfth annual report recently issued, is very encouraging, and offers hope that the cause of this dread disease may before long be ascertained.

Study and treatment of cancer by proteolytic enzymes: preliminary report (H. C. Connell)—*C.M.A.J.*, Oct. '35, p. 364.

Editorial comments on Connell's paper.—*C.M.A.J.*, Oct. '35, p. 428; *J.A.M.A.*, Oct. 5, '35, p 1122; *Lancet*, Oct. 19, '35, p. 898; *B.M.J.*, Oct. 26, '35, p 791.

Aetiology of cancer of the skin (A. R. Somerford)—*B.M.J.*, June 29, '35, p. 1305.

Induction of cancer by cracked mineral oils (Twort and Twort)—*Lancet*, Nov. 30, '35, p 1226.

Treatment of mammary cancer (H. M. Moran)—*B.M.J.*, Nov. 9, '35, p. 889.

Lead chemotherapy (J. A Bargen *et al*)—*Amer. J. Cancer*, Apr. '35, p. 762

Cobra venom: effect on malignant tumours (J. Lavedan)—*Paris méd*, Mar 16, '35, p. 221

Short wave therapy (R G Canti).—*Brit. J. Phys. Med*, May '35, p. 18.

DIABETES MELLITUS.

A full review of the literature on diabetes was given in our issue of December: this recorded all developments to time of going to press, and since then little of importance has appeared The extra references given below were received too late for inclusion in the December review.

Abstract review of literature to November. types; incidence; heredity; associated conditions; sugar tolerance test; diabetes in childhood; complications; diabetic coma; insulin treatment; dietetic treatment; miscellaneous remedies; synthalin; galega; parathyroid extract; duodenal extract; muscular exercise—PRESCR, Dec. '35, pp. 367-379

Blood sedimentation rate in diabetes mellitus (*D. W. Kramer*).—*J.L.C.M*, Oct. '35, p. 37.

Intravenous injection of insulin: clinical and experimental study (Guarino and Stellatelli).—*Gior. clin. med*, Aug. 10, '35, p. 1132.

DIPHTHERIA.

This disease continues to occupy the attention of workers, but while reports have been fairly numerous nothing has occurred that is startlingly new. The use of alum-precipitated toxoid has received further attention, and as a means of inducing immunity it appears

to be very satisfactory Prevention of diphtheria by swabbing or spraying the throat with petrol has been suggested

Evaluation of modern prophylactics (C J McSweeney)—*B M J*, Jan 19, '35, p 103

Diphtheria in the tropics a subclinical disease in negroes (G Kinneard)—*B M J*, Feb 2, '35, p 201

Malignant diphtheria diagnosis and treatment (B A Peters)—*B M J*, Mar 23, '35, p 585

Methods for identification of diphtheria bacilli and of carriers (M B Brahdy *et al*)—*J.A M A*, May 25, '35, p 1881

Autogenous vaccine for diphtheria carriers (A C Guthrie)—*B M J*, Aug 24, '35, p 341

Prevention by swabbing or spraying throat with petrol (G A Stephens)—PRESCR, Dec '35 p 366

Experiences with Schick test in active immunization (Gundel and Wüstenberg)—*D m W*, Nov 22, '35, p 1871

Schick immunity and diphtheria infection (E A Underwood)—*Lancet*, Feb 16, '35, p 364

Schick test and active immunization in relation to epidemic diphtheria (Parish and Wright)—*Lancet*, Mar 16, '35, p 600

Immunization some immediate and final issues (G Bousfield)—*Practitioner*, Dec '35, p 821

Alum precipitated diphtheria toxoid review of recent literature—PRESCR, July '35, p 239

Passive immunity in infants and their response to toxoid (Greengard and Bernstein)—*J A M A*, Aug 3, '35, p 341

Cure and prevention some immunological aspects (J Menton)—*B M J*, Aug 10, '35, p 246

Antigenic value of various preparations of toxoid (C E Healey)—*J A M A*, Oct 12, '35, p 1182

Reduction of diphtheria following 3 doses of toxoid (McKinnon and Ross)—*J A M.A*, Oct 26, '35, p 1325

Prevention by 'one shot' method alum precipitated toxoid (M Naughten *et al*)—*B M J*, Nov 9, '35 p 893

Use of alum precipitated toxoid in immunization (J E Haine)—*B M J*, Nov 9, '35, p 896

DYSENTERY.

The flood of literature that followed the outbreak of amoebic dysentery in Chicago in 1933 has subsided, and there is little now to record A few articles of a general character have dealt with both amoebic and bacillary dysentery, but nothing new has developed

Amoebic—Diagnosis and treatment (T T Mackie)—*N Y St J M*, Mar 15, '35, p 261

Dangers of incorrect diagnosis (E P Hogan)—*Am J Surg*, May '35, p 498

Chronic amoebiasis and chronic appendicitis (W Wilkinson)—*B M J*, Sept 7, '35, p 452

Results and dangers in treatment 15 years' experience at Mayo Clinic (P W Brown)—*J.A.M.A.*, Oct 26, '35, p 1319

Colonic irrigation with weak copper sulphate (P Beregoff)—*C.M.A.J.*, June '35, p 641 (P Nov 358)

Bacillary—Summary of treatment and statistics of an epidemic (H W Corner)—*B.M.J.*, June 8, '35, p 1162

Oral immunization review of literature (Thomson and Thomson)—*Med Press*, Aug 14 '35, p 133

EAR, NOSE, AND THROAT.

While most of the literature dealing with ear, nose, and throat work belongs properly to the domain of surgery, certain work of a therapeutic nature must be recorded This reveals little that is new, but the articles are all of a practical nature

Otitis media as complication of scarlet fever (discussion)—*Lancet*, June 22, '35, p 1444

Discharging ears treated by iodine and boric acid powder (R H Bettington)—*M.J. Australia* June 15, '35, p 747

Otorrhoea prognosis (W Howarth)—*Lancet*, Nov 9, '35, p 1071

Chronic suppurative otitis media treatment (L G Brown)—*B.M.J.*, Nov 23, '35, p 986

Chronic suppurative disease of the middle ear and its complications (J P Stewart)—*Med Press*, Nov 20, '35, p 454

Acute suppurative otitis media and mastoiditis diagnosis and treatment (N Patterson)—*Practitioner*, Nov '35, p 619

Middle ear suppuration conservative treatment (F J Clemmson)—*Practitioner*, Nov '35, p 629

Chronic pyogenic inflammation of maxillary antrum and other nasal accessory sinuses Semon lecture (H Tilley)—*Med Press*, Feb 13, '35, p 148

Intranasal ionization for sinusitis, ozaena, etc. (P Franklin)—*Med Press*, Mar 20, '35, p 281

Nasal sinusitis and infection of the eyeball (E Watson-Williams)—*P.R.S.M.*, Oct '35, p 1584

Laryngeal tuberculosis treatment (J Dundas Grant)—*Med Press*, Apr 17, '35, p 366

ENDOCRINOLOGY.

The latest advances in endocrinology were fully recorded in the special number of THE PRESCRIBER issued in May of last year The issue, which contains matter of exceptional interest, is still available, price 3s 6d post free

EYE DISEASES

Cataract caused by dinitrophenol has been the subject of numerous articles in which this condition has been very fully discussed Other

articles of a practical nature dealing with treatment of eye conditions have appeared, but little that is new has been reported

Cataract following use of dinitrophenol (2 articles and editorial)—*J.A.M.A.*, July 13, '35

Ditto (4 articles)—*J A M A*, Sept 17, '35

Glaucoma some newer conceptions (P A Harry)—PRESCR, July '35, p 221

Detachment of the retina (P A Harry)—PRESCR, Nov '35, p 341

Detachment of the retina (Kronfield and Luo)—*Chinese M J*, Aug '35, p 723

Embolism of retinal artery acetylcholine injections (Orr and Young)—*B M J*, June 1, '35, p 1119

Glaucoma medical aspects and early diagnosis (H M Traquair)—*B M J*, Nov 16, '35, p 933

Allergic conjunctivitis spring catarrh and allied conditions (H Lagrange)—*B J Ophthal*, May '35, p 241

Treatment of eye affections with gold sodium thiosulphate (I J Koenig) *N Y St J M*, Oct 15, '35, p 1019

Retinitis treated by protein shock (D Simpson)—*B M J*, Nov 23, '35, p 997

The sinuses in relation to eye disease (E R Chambers)—*P R S M*, Oct '35, p 1582

Nasal sinusitis and infection of the eyeball (E Watson Williams)—*P R S M*, Oct '35, p 1584

FOOD POISONING.

The outstanding event during 1935 has been the occurrence in north London in August of several cases of botulism Since the outbreak at Loch Maree in 1922 no other cases have been recorded in this country The two cases reported by Templeton were both fatal, the subjects being two sisters who died within eight hours of one another and within forty-eight hours of the onset of symptoms The symptoms followed consumption of 'nut-meat brawn,' a vegetable mixture put up in glass containers, but the manufacturers were absolved from any charge of neglect The outstanding symptoms were giddiness, vomiting, and ocular paralysis Anti botulinus serum was given, but without avail A gram-positive organism having the characteristics of *B botulinus* was isolated from the suspected food

In the case reported by Kitcat the eye symptoms were less pronounced, but vomiting was incessant and death occurred within twenty one hours of taking the affected food, also 'nut meat brawn' In the fourth case the diagnosis was doubtful

An outbreak of bacterial food poisoning occurred at Swansea in September, following a 'treat' given to a number of poor children The symptoms were headache, diarrhoea, and vomiting, with raised temperature The infecting organism is believed to have been one of the Salmonella group

Two fatal cases of botulism (W L Templeton)—*B.M.J.*, Sept 14, '35, p 500

A fatal case of botulism (C de W Kitcat)—*B M J*, Sept 28, '35, p 580

A case of botulism bacteriological examination of suspected food (Lane and Jones-Davies)—*Lancet*, Sept 28, '35, p 717

Series of outbreaks of food poisoning at Cardiff (C W Anderson *et al*)—*Lancet*, Feb 2, '35, p 285

Unusual outbreak of gastro enteritis (J Fanning)—*B M J*, Mar 29, '35, p 583

Bacterial food poisoning outbreak at Swansea (Edit)—*B M J*, Sept 28 '35 p 589

Outbreak at Indianapolis apparently due to staphylococci (G M Dack *et al*)—*J A M A*, Nov 16, '35, p 1598

GASTRIC DISEASES.

Peptic ulcer still bulks largely in the literature dealing with gastric diseases Much interest has been shown in the treatment with histidine, the brand used in all the cases being 'Larostidin' (Roche) This is a 4 per cent solution of histidine monohydrochloride, it is given by intramuscular or subcutaneous injection, the dose being 5 ml daily for several weeks Reports from several countries (see below) testify to its efficacy Oral administration of larostidin is said to have given good results in cases of persistent flatulence, tablets of 0 2 gm are used

Histidine treatment of peptic ulcer (E Bulmer)—*Lancet*, Dec 8, '34 p 1276 (P June 213)

Histidine treatment of peptic ulcer of lesser curvature 12 cases (D Smith)—*B M J*, July 27, '35, p 154

Histidine monohydrochloride in gastro duodenal ulcer (Volini and McLaughlin)—*Med Record*, Apr 17, 35, p 364

Histidine in peptic ulcer (J T Eads)—*Am J Dig Dis*, Sept '35, p 426

Histidine in 46 cases gastro duodenal ulcer (E E Bauke)—*D m W*, Sept 20 '35, p 1510

Histidine in peptic ulcer (J W Könıng)—*S m W*, Oct 19, '35, p 1006

Histidine in gastro duodenal ulcer (E Aron)—*Presse méd*, July 27, '35, p 1195

Alkalosis arising in treatment of peptic ulcer (W Oakley)—*Lancet*, July 27, '35, p 187

GOITRE

The literature on goitre is closely bound up with that on the thyroid gland, which is very voluminous A full review of thyroid disorders appeared in our issue of May 1935 and a similar review will appear in May of this year

GONORRHOEA.

The literature on gonorrhoea presents little, if anything, that is new, most communications being either of a general character or dealing with remedies already tried, such as silver, acriflavine, mercurochrome, etc Gonococcal vaginitis has been successfully treated by means of the female sex hormone In gonorrhoeal arthritis artificial fever therapy has given good results A new arsenic and acridine compound 'mesodine' (Bayer) has been introduced for the treatment of cervical gonorrhoea in women A 2 per cent aqueous solution is instilled, this is said to be of value also in rectal and urethral infection

Experiences with gonococcus filtrate and other forms of intradermal therapy (Cumming and Burhans) —*J A M A*, Jan 19 '35, p 181

Surgical complications indications and methods (A E Goldstein) —*J.A M.A*, Mar 9, '35, p 800

Gonococcal arthritis general article (R S Woods) —*B J V.D*, July '35, p 157

Gonorrhoeal arthritis artificial fever therapy, 31 cases (H W Kendell *et al*) —*Amer J Surg*, Sept '35, p 428

Gonorrhoeal vaginitis 2 years' experience of treatment with theelin or female sex hormone (J R Miller) —*Am J O G*, Apr '35, p 553

Effect of theelin on human vaginal mucosa (R M Lewis) —*Am J O G*, June '35, p 806

Gonorrhoeal vaginitis unsuccessful treatment with ovarian hormone (J T Witherspoon) —*Am J O G*, June '35, p 906

Gonococcal vaginitis successful treatment with amniotin suppositories (TeLinde and Brawner) —*Am J O G*, Oct '35, p 512

HAEMORRHAGE.

The announcement made in 1934 of the effectiveness of snake venom (*Vipera russellii*) in haemophilia has been carried a step further Clinical trials with the diluted venom (1 10,000) have given most encouraging results in haemophilia when applied locally to the bleeding spot Trials in America with the venom of the moccasin snake (*Ancistrodon piscivorus*) have been reported, subcutaneous injections (0 2 to 1 0 ml of a 1 3000 solution) being effective in controlling various haemorrhagic conditions unassociated with blood changes In thrombocytopenic purpura it seems to be effective in some cases and ineffective in others, it is of no value in congenital haemophilia

The successful employment of congo red as a haemostatic has been reported It is given by intravenous injection, the dose being 10 ml of a one per cent solution

The treatment of haemoptysis (G E Beaumont) —*B M J*, Jan 5, '35, p 25

Treatment of haematemesis and melaena with food (E. Meulengracht) —*Lancet*, Nov 30, '35, p 1220

Radium therapy useful in uterine haemorrhage, particularly at menopause —*M R C Report No* 204 (Med Uses of Radium)

Treatment of epistaxis in children (E Wessly) —*W k W*, Oct 4, '35, p 1214

Haemophilia intravenous transfusion of unmodified blood (Jones and Tocantins) —*J A M A*, Dec 1, '34, p 1671 (P Feb 48)

Haemostatic uses of snake venom (B Barnett) —*P R S M*, Sept '35, p 1469

Moccasin snake venom in haemorrhagic conditions (Peck and Rosenthal) —*J A M A*, Mar 20, '35, p 1066 (P Oct 336)

Snake venom in purpura (H M Greenwald) —*Am J Dis Ch*, Feb '35, p 347 (P Oct 336)

Moccasin snake venom in nasal haemorrhage (S Dack) —*J A M A*, Aug 10, '35, p 412 (P Oct 336)

Snake venoms in therapeutics (Chopra and Chowhan) —*I M G*, Aug '35, p 445

Congo red in haemoptysis —Abstr Prescr, Feb '35, p 48

Intestinal haemorrhage during typhoid use of congo red (F Szirmai) —*M m W*, Aug 30, '35, p 1403

HELMINTHIASIS

Considerable work has been done in connexion with helminthiasis, but with the exception of certain pharmacological experiments with hookworm-killing drugs little can be gathered regarding treatment Hookworm anaemia is referred to under anaemia

Hookworm infection in the Punjab (Yacob and Chaudhri) —*I M G*, Dec '34, p 669

Passage of hookworms after treatment (Maplestone and Mukerji) —*I M G*, June '35 p 320

Hookworm disease grave risks as complication of pregnancy (G A W. Wickramasuriya) —*J Obst & Gyn Brit Emp*, Apr '35, p 217

Hookworm appraisement of hookworm killing drugs (C Lane) —*Lancet*, June 22, '35 p 1459

Hookworm administration of carbon tetrachloride for (A S Tuxford, C Lane) —*Lancet*, June 1 and 8 '35, pp 1302, 1357

Schistosomiasis chemotherapy with antimonials (M Khalil Bey) —*J Egyp M Assoc*, Apr '35, p 284

INFLUENZA

The disease, or group of diseases, known as influenza, is still the subject of investigation, but beyond the assumption that it is due to a filterable virus little is known of its cause Experiments on animals are throwing some light on the matter, but nothing very definite has as yet been recorded

The periodicity of influenza (B E Spear) —*Lancet*, Dec 15, '34, p 1331

Minor epidemics of 'influenza' (epidemic catarrh) (G M Wauchope) —*Lancet*, Apr 13, '35, p 879

Recent advances in the study of influenza (T Francis)—*J A M A*, July 27, '35, p 251

Effect of influenza epidemics on the certified causes of death (P Stocks)—*Lancet*, Aug 17, '35, p 386

LEPROSY.

The literature on leprosy of the past two years was fully reviewed in our issue of November last, pp 345-357, and a lengthy bibliography was appended Several publications are now devoted exclusively to this subject, and mention may be made of the *International Journal of Leprosy*, published in Manila and now in its fourth year

MALARIA.

The great epidemic in Ceylon has been the outstanding topic of the year, although it reached its peak in December 1934 The epidemic attacked nearly half a million of the population and exacted a heavy toll in life Some account of it was given in our review in September, and only now are full details becoming available The epidemic afforded an opportunity for clinical trial of the newer antimalarial remedies on a large scale

The flocculation test introduced some years ago by Henry has been studied further and has given rise to some controversy, details of which were given in our recent review Research on the quinoline compounds is still being pursued with a view to the synthesis of bases analogous to quinine The cinchona alkaloids, including the mixture known as totaquine, have been studied further Atebrin and the new soluble form for injection known as 'atebrin-musonat' have received attention ('Musonat' is the latinized form of a German name it does not mean a salt of musonic acid as some writers seem to think—there is no such acid) A number of new synthetics have been tested clinically, but so far no marked superiority over quinine or atebrin has been definitely proved

The use of malaria in the treatment of general paralysis is referred to under syphilis A full review of the treatment of malaria appeared in our issue of September last, pp 271-284, and the following are the more important references that have come to hand since

Review of literature to date—PRESCR, Sept '35, p 271

History of malaria prevention (M Watson)—*Glasgow M J*, Feb, Mar, and Apr '35, pp 49, 130, 202

Congenital malaria (Tanner and Hewlett)—*Lancet*, Aug 17, '35, p 369

Note on the pathology of *P knowlesi* infection in man (Rooyen and Pile)—*B M J*, Nov 2, '35, p 840

The epidemic in Ceylon—*Lancet*, Nov 9 and 23, '35, pp 1077, 1176, *B M J*, Nov 23, '35, pp 1001, 1015 (P Sept 271)

Some interesting cases occurring during epidemic in Ceylon (S de Silva)—*J Trop Med*, Mar 15, '35, p 66

Diagnosis —Henry's reaction several papers —*C.R Soc biol*, 1935 cxviii 1076 1332, 1334, 1336, 1443, 1573

Cinchona Alkaloids —Relative clinical efficacy of totaquine and quinine (Hicks and Chand) —*I.M G*, Oct '35, p 579, from *Records of Malaria Survey of India*, Mar '35, p 39

Atebrin —Clinical investigation of treatment by atebrin musonat injections (E C Vardy) —*Malayan M J*, Sept '35, p 67

Death after injection of atebrin musonat (Fernando and Wijerama) —*Lancet*, Nov 9 '35, p 1056

Blackwater Fever —Case in a negro child (C C Chesterman) —*Lancet*, Sept 7, '35, p 554

A case of quinine haemoglobinuria (R N Chopra *et al*) —*I M G*, Aug '35, p 453

Atebrin in treatment of blackwater fever (I Goldblatt) —*S.Af M J*, June 8, '35, p 384 (P Sept 278)

Calcium treatment of blackwater fever (W van Slype) —*Bull Soc path exot*, Feb 13, '35, p 85

Laboratory studies a new blood pigment (Fairley and Bromfield) —*Trans Roy Soc Trop Med*, Nov 27, '34, p 307

MEASLES.

During the past few years several new agents have been advocated for the treatment and prevention of measles Convalescent serum has had a vogue, as also has amidopyrine, but of these comparatively little has been heard recently Placental extract, mentioned as a prophylactic by American workers in 1933 and referred to in our pages at the time, has made a step forward, though it is still to be regarded as in the experimental stage The extract is made from human placentas, known to be healthy, which are ground up and extracted with saline, it is precipitated with ammonium sulphate, dialysed, and adjusted for protein nitrogen strength It is given by intramuscular injection Placental extract is obtainable commercially in the United States, where it is known as 'immune globulin (human)' or 'placimmunin' Reports show that as a prophylactic it is at least as effective as convalescent serum, but reports deal with only a limited number of cases, and it is admittedly impossible to test adequately the value of any agent merely as a prophylactic The Council on Pharmacy and Chemistry of the A M.A, while regarding immune globulin as a promising immunizing agent, considers that more evidence of its value is needed before it can confidently be recommended

Treatment general article (W Gunn) —*B.M J* Mar 23 '35, p 597

Attenuation of measles by adult serum (W S Burnet) —*Lancet*, Mar 16, '35, p 631

Epidemiological factors in prophylaxis (Karelitz and Schick) —*J A M A*, Mar 23, '35, p 991

Factors influencing effectiveness of placental extract in modification of measles (C F McKhann *et al*) —*J Pediat*, May '35, p 603

Treatment, modification, and prevention by use of immune globulin (I. M. Levitas).—*J.A.M.A.*, Aug. 17, '35, p. 493.

Report on immune globulin by Council on Pharmacy and Chemistry of the A.M A.—*J.A.M.A.*, Aug. 17, '35, p. 510.

Placental extract in measles prophylaxis (Edit.).—*Lancet*, Sept. 28, '35, p. 728 (P. Sept. '33, p. 290).

Treatment with pentnucleotide (Smith and Quigley).—*Amer. J. Dis. Ch.*, Jan. '35, p. 91.

PNEUMONIA.

In the treatment of pneumonia reliance is now generally placed on serum therapy, and more stress is laid on the necessity for typing in order to ascertain the appropriate serum. So employed, serum treatment of type I pneumonia is said to be both specific and effective, with certain limitations. Special attention is directed to the article by Davies and co-workers, referred to below, in which the subject is very exhaustively treated.

A study of pneumococcal pneumonia: three articles (D. T. Davies *et al.*).—*Lancet*, Apr. 6, 13, and 20, '35, pp. 791, 849, 919.

Acute lobar pneumonia (J. W. Linnell).—*Practitioner*, Jan. '35, p. 39.

Lobar pneumonia and digitalis (Cohn and Lewis).—*Am.J.M.Sc.*, Apr. '35, p. 457.

Acute lobar pneumonia: serum therapy (McCrie and Murray Lyon).—*Edinb. M.J.*, Apr. '35 (Med.-Ch. Soc.), p. 37.

Lobar pneumonia: serological treatment (J. M. Johnston).—*Edinb. M.J.*, May '35, p. 265.

Convalescent serum in acute pneumonia (R. Priest).—*J.R.A.M.C*, Feb. '35, p. 121.

General treatment (W. H. Palmer).—*S.Af.M J.*, Apr. 27, '35, p. 259.

Serum treatment (H. L. Heimann).—*S.Af.M.J.*, Apr. 27, '35, p. 261.

Artificial pneumothorax in acute lobar pneumonia (Hines and Bennett).—*Arch. Int. Med.*, Jan. '35, p. 100.

Artificial pneumothorax in lobar pneumonia (Holmes and Randolph).—*Ann. Int. Med.*, Mar. '35, p. 1008.

Treatment with solvochin and calcium (K. Nissen).—*D.m.W.*, Feb. 22, '35, p. 295.

PSITTACOSIS.

Since this subject was reviewed in our issue of June 1930, little has been added to the knowledge of the disease, a full account of which is given also in the Ministry of Health Report No. 61, 1930. Cases, it seems, have been occurring in this country during the past few years in spite of the embargo on the import of parrots. The causal agent is believed to be a virus, but as yet little is known regarding it.

Recent observations on psittacosis (W. Levinthal).—*Lancet*, May 25, '35, p. 1207.——Editorial.—*Ibid.*, p. 1226.

Psittacosis in developing egg (Burnet and Rountree).—*J. Path. & Bact.*, May '35, p. 471.

Psittacosis in Australian parrots (F. M. Burnet)—*M.J. Australia*, Dec. 8, '34, p. 743.

Growth and development of virus in tissue cultures (Bland and Canti).—*J. Path. & Bact*, Mar. '35, p. 231.

Influenzal conditions in respiratory passages and lungs (H. von Hoesslin)—*D.m W.*, Feb. 8, '35, p. 213.

Diagnosis by injection of sputum into mice (Rivers and Berry)—*J. Exper. Med.*, Feb. '35, p. 205.

RHEUMATISM.

The group of diseases known as rheumatic have been the subject of extensive study and much speculation. Innumerable remedies have been advocated, most of them merely palliatives, and in the absence of more exact knowledge regarding causes only palliatives are possible. Spa treatment and physical therapy still stand in favour: our issue of March was devoted to that subject. Of the more empirical remedies, bee-venom still attracts attention, while gold salts have been the subject of not a few communications. Histamine and artificial pyrexia are also favoured.

Rheumatism and its results (K. D. Wilkinson)—*Lancet*, Aug. 24, '35, p 411.

Plasma proteins and non-protein nitrogen, and the sedimentation rate in chronic rheumatic disorders (Aldred-Brown and Munro)—*Q.J.M.*, July '35, p 269

Dietetic study of cases of juvenile rheumatism (E. C. Warner *et al.*).—*Q J.M*, July '35, p 227

Institutional methods in chronic rheumatism (M. B Ray)—*Practitioner*, Feb '35, p. 147.

Spa treatment of chronic rheumatic conditions (G. Holmes)—*Practitioner*, Feb '35, p 159.

Accessory treatment at spas (G. L. K Pringle)—PRESCR., Mar. '35, p. 75.

Diet and spa treatment (A G. Watson)—PRESCR., Mar. '35, p. 81.

After-effects of spa treatment (G. R. P. Aldred-Brown)—*B J. Phys. Med*, Mar. '35, p 215.

Effects of artificial heat on circulation in cold temperate climates (R F. Fox).—*B.M.J.*, Apr. 6, '35, p. 698.

Natural mud treatment · 106 cases (L. Justin-Besançon).—*Paris méd*, Apr. 20, '35, p. 345.

Rheumatic heart disease and vitamin C (C. B. Perry)—*Lancet*, Aug. 24, '35, p 426

Gold therapy in arthritis: abstracts of articles by Slot (*Practitioner*, June '35, p. 788), Pemberton (*Lancet*, May 4, '35, p. 1037), and Hartfall and Garland (*Lancet*, July 6, '35, p. 8)—PRESCR, Sept. '35, p. 289.

Malaria therapy in rheumatoid arthritis (R. L. Cecil *et al.*)—*J.A.M.A.*, Oct. 12, '35, p. 1161.

Fever therapy: results (P. S. Hench *et al.*).—*J.A.M.A.*, May 18, '35, p. 1779.

Sulphur therapy of chronic rheumatism (M Loeper)—*S.m W*, Dec 8, '34, p 1122

Colloidal sulphur in chronic arthritis (W B Rawls *et al*)—*Am J.M Sc*, Sept '35, p 400

Acetylcholine intramuscularly in arthritis deformans (Arbat and Piulachs)—*Rev med Barcelona*, May '35, p 388 (P Nov 358)

RICKETS.

It is now generally held that rickets is due to deficiency of vitamin D, and various forms of this vitamin are now largely used both for prevention and for treatment A case is recorded in a German journal in which a child developed rickets in spite of a diet rich in vitamins, but details of the child's feeding show that the diet was almost entirely vegetable, even the milk was made from almonds Much of the work during the past year has been biochemical and experimental, but a selection of the more practical contributions is given below

New aspects of deficiencies in nutrition (D Hunter)—*Lancet*, May 4, '35, p 1025

Renal dwarfism and late rickets (R W B Ellis)—*Lancet*, Jan 19, '35, p 142, (Edit) *Ibid*, Jan 26, '35, p 221

Signs of rickets, also non rachitic bowing of legs (W Sheldon)—*Lancet*, Jan 19, '35, p 134

Adult rickets (osteomalacia) and foetal rickets further studies (J P Maxwell)—*P.R.S.M*, Jan '35, p 265

Development of rickets in a child fed with diet rich in vitamins but almost entirely vegetable (K Oxenius)—*D m W*, Dec 21, '34, p 1953

Comparison of antirachitic potency of cod liver oil and irradiated ergosterol (W C Russell *et al*)—*J Nutrition*, May '35, p 569

Comparison of 'yeast milk' and irradiated milk (E T Wyman *et al*)—*N Eng J.M*, Feb 7, '35, p 257

Comparative antirachitic value of irradiated cow's milk and of milk from cows fed with irradiated yeast (H J Gerstenberger *et al*)—*J A.M.A*, Mar 9, '35, p 816, correction Apr 13, '35, p 1348

Antirachitic value of irradiated evaporated milk (M Rapoport *et al*)—*J Pediat*, June '35, p 799

Clinical status of vitamin D milks (Bunker and Harris)—*N Eng J M*, Dec 20, '34, p 1140

Dermal absorption of vitamin D—irradiated ergosterol (Astrowe and Morgen)—*Amer J Dis Ch*, Apr '35, p 912

Clinical experiences with crystalline vitamin D (calciferol) influence of menstruum on effectiveness of antirachitic factor (J M Lewis)—*J Pediat*, Mar '35, p 362

Vitamin D content of vegetable oils and their value in rickets (Berzaczy and Rupilius)—*W k W*, Nov 30, '34, p 1449

Irradiated cholesterol in human rickets (F F Tisdall *et al*)—*C.M.A J*, May '35, p 490

Phosphorus not antirachitic (Lecoq and Gallier)—*C R Soc biol*, 1934, cxvi, 1383

SCARLET FEVER.

Immunization is the theme of most of the literature on scarlet fever during the past year The employment of the Dick test and the production of immunity are discussed by a number of workers in various aspects, but nothing startlingly new has been recorded

Recurrent cases (J R Heming)—*Lancet*, Feb 2, '35, p 264
Three attacks within 4 months (J Todesco)—*Lancet*, Mar 9 '35, p 548
Treatment (A Joe)—*B M J*, Mar 9, '35, p 483
Prevention of secondary infection of tuberculous joints (M C Wilkinson)—*Lancet*, Dec 29, '34, p 1446
Diphtheria cross infection in a scarlet fever ward (T Seager)—*Lancet*, May 25, '35, p 1243
Convalescent scarlet fever serum prophylactic and therapeutic value in 2875 cases (A L Hoyne *et al*)—*J A M A*, Sept 7, '35, p 783
Dick test specificity (H E Smiley)—*J L C M*, Mar '35, p 589
Dick test effect of placental extract on (A Ross)—*J Pediat*, Apr '35, p 546 (*see* Measles)
Dick test variability in strength of toxin (A Friedman *et al*)—*J A M A*, Sept 21, '35, p 956
Active immunization (Benson and Rankin)—*Lancet*, Dec. 15, '34, p 1357
Preventive immunization (J Litt)—*Lancet*, Apr 20 '35, p 932
Preventive immunization in an institutional epidemic (Scott and Morton)—*B M J*, Jan 5, '35, p 12
Attempted immunization in a public school (L R Lempriere)—*B M J*, Sept 7, '35, p 450
A study of active immunization in charitable institutions and public schools (J N Henry)—*J A M A*, Aug 17, '35, p 488

SKIN DISEASES

A lengthy review on Dermatology appeared in our issue of October 1935, it was followed in the same issue by several pages of useful skin prescriptions This brought the subject to date, the references below are to articles that have appeared since that review was written

The literature on dermatology is voluminous, but very little fresh ground is broken A group of diseases caused by streptococci has been described, for which the term 'streptococcal dermatitis' has been suggested Thioglycerol, a stable sulphydryl (SH) compound, has been introduced for the treatment of ulcers 'Urinary proteose' has been still further discussed, and its existence as a definite compound has been questioned

The cause of *acne* has been further investigated, and the opinion is gaining ground that it is primarily due to endocrine agency, especially the acne of adolescence Treatment of *burns* with cod-liver oil has several advocates *Calcinosis* has been the subject of several articles *Dermatitis*, especially contact dermatitis in its

application to industry, has received considerable attention Limitation of the term *eczema* to a definite type of eruption has been advocated *Fungus infections*, particularly of the feet, have been studied further The relative merits of gold and bismuth in treatment of *lupus erythematosus* have been discussed Dermatologists are still baffled by *psoriasis*, notwithstanding numerous remedies for which success has been claimed

Abstract review—dermatology, general chemistry of the skin, septic infections, light sensitization, allergy, streptococcal dermatitis, x ray therapy, colloidal sulphur, thioglycerol, urinary proteose—PRESCR, Oct '35, pp 295 300

Abstract review—skin diseases acne, alopecia, burns, calcinosis, cheiropompholyx, dermatitis, eczema, erysipelas, erythema nodosum, fungus infections, furunculosis, granuloma annulare, impetigo, lupus, monilethrix, oriental sore, pemphigus, pigmentation, pruritus, psoriasis, purpura, tularaemia, ulcers, urticaria, varicose veins, warts—PRESCR, Oct '35, pp 300-332

Useful skin prescriptions—PRESCR., Oct '35, pp 332 335

Recent References

General.—Incidence of skin conditions in Australia (H Lawrence)—*B M J*, Sept 28, '35, p 572

Skin disinfection (Edit)—*Lancet*, Oct 12, '35, p 838

Acid in the blood as a cause of diseases of the skin (J L Ginsberg)—*Arch D & S*, Sept '35, p 464

Dystrophic conditions of the nails seen with general diseases (A D Heath)—*Med Press*, Sept 25, '35, p 281

Acne—Treatment with pregnancy urine extract prelim report (Lawrence and Feigenbaum)—*N Eng J M*, June 27, '35, p 1213

Oestrogenic substance in the blood of patients with acne (Rosenthal and Neustaedter)—*Arch D & S*, Oct '35, p 560

Anthrax.—Treatment by local carbolic injections (G C Dorling)—*Chinese M J*, July '35, p 662

Burns—Treatment (A C Turner)—*B M J*, Nov 23, '35, p 995

Calcinosis—Improvement occurring in cases in children (F P Weber)—*B J.D & S*, Oct '35, p 400

Erysipelas—Incidence of (J Riddell)—*B.M J*, Nov 16, '35, p 946

Anti scarlatinal serum in erysipelas (W H Brazil)—*B.M J*, Nov 2, '35, p 840

Erythroedema—Pink disease (Wood and Wood)—*B M J*, Sept 21, '35, p 527

Observations on six cases (C F Harris)—*St Barth Hosp Rep*, 1935, lxvii, 137

Fungus Infections—Inhalations of ethyl iodide in (J H Swartz)—*Arch D & S*, Oct '35, p 551

Actinomycosis unusual case in the hand (R S Hollingsworth)—*J.A.M A*, Oct 19, '35, p 1266

Ringworm of the scalp in India (Dey and Maplestone)—*I M G*, Oct '35, p 541

Improved source of ultraviolet rays for diagnosis of ringworm of the scalp (A M Davidson *et al*)—*C M A J*, Nov '35, p 534

Furunculosis —Treatment of boils and carbuncles (P K Fraser) —*B M J*, Nov 9, '35, p 894

Lupus Vulgaris.—New method of treatment intradermal injection of phenyl ethyl hydnocarpate (N Burgess) —*B M J*, Nov 2, '35, p 835

Naevi —Radium treatment (N S Finzi) —*B M J*, Sept 28, '35, p 571

Oriental Sore.—Observations on dermal leishmaniasis (Smith and Halder) —*I M G*, Oct '35, p 544

Pigmentation.—Occupational argyria (Harker and Hunter) —*B J D & S*, Nov '35, p 441

Psoriasis —Treatment with organic sulphur compound—chiefly allyl sulphide (F M Thurmon) —*N Eng J M*, Aug 22, '35, p 353

Purpura.—General article (H M Oddy) —*Med Press*, Oct 9, '35 p 314

Essential purpura haemorrhagica (B Myers) —*B M J*, Sept 7, '35, p 445

Scabies —Outbreak in a mental hospital (F E Kingston) —*Lancet*, Oct 12, '35, p 815

Tularaemia.—Two cases (F K Wright) —*C M A J*, Sept '35, p 309

Urticaria —Therapy of urticaria and angioneurotic oedema (Fantus and Cornbleet) —*J A M A*, Aug 24, '35, p 595

Warts —Infective warts and their treatment (Ghosh and Maplestone) —*I M G*, Aug '35, p 441

SYPHILIS.

The treatment of early syphilis has been the subject of an inquiry by the League of Nations Health Organization, investigations having been made in five countries—Denmark, France, Germany, Great Britain, and the United States Reports from ninety three clinics were received and over 13,000 case records were analysed, and as a result certain recommendations were formulated A summary of these was given in the review on Syphilis in our issue of August last The results of a five-years' study of latent syphilis, conducted by the Group Clinics of five leading American universities, have also been reported An effort to evaluate the various serological tests has been made by a body of American workers, the results of which were less conclusive than one might have expected An immense amount of work is being done in connexion with these diagnostic tests, and still every worker prefers his own method, using some other method as a check in doubtful cases

Further study has led to a better understanding of the toxic effects produced by the arsphenamine compounds, so that prevention and treatment of such accidents are now comparatively simple Bismuth therapy is much in favour, and particular interest is being shown in the liposoluble preparations In the treatment of neurosyphilis tryparsone (tryparsamide) is still regarded with favour, though caution is necessary on account of its tendency in some cases to produce optic atrophy The employment of malaria and other

methods of inducing pyrexia is being increasingly recognized, especially in the treatment of general paralysis Malaria is generally regarded as giving the best results, in cases where it is impracticable or undesirable, other methods of inducing pyrexia may be employed These are safer than malaria, but it is generally believed that they are less effective therapeutically

All these and other points were fully discussed in the review already mentioned as appearing in our August issue More recent references are given below

Abstract review causal organism, treatment of early syphilis, latent syphilis, diagnostic reactions, arsphenamine compounds, bismuth therapy, mercury, neurosyphilis —PRESCR, Aug '35, pp 247 264

Recent References

General —Syphilis and pregnancy clinical study of 2150 cases (J R McCord) —*J.A M A*, July 13, '35, p 89

Congenital syphilis results of treatment in children (F R Smith) —*J.A M.A*, Aug 10, '35, p 409

Therapeutic use of iodides (W R Snodgrass) —*Q J M*, July '35, p 247

Role of iodine in therapy of syphilis relationship to lipoids (E T Burke) —*Arch D & S*, Sept '35, p 404

Treatment with spirochaete vaccine (Hilgermann) —*M.m W*, Nov 1, '35, p 1760

Diagnostic Reactions —Value of serum reactions in diagnosis and treatment (T E Osmond) —*B J V D*, July 35 p 177

A rapid test for syphilis (G F Laughlen) —*C M A J* Aug '35, p 179

Evaluation of tests in State and local laboratories (Edit) —*J A M A*, July 27, '35, p 286

Value of Kline's micro test (J Schmitz) —*Klin Wschr*, Sept 14 '35, p 1320

Some aspects of Meinicke s clarification reaction (F Koch) —*D m W*, July 19, '35, p 1153

Diagnostic value of Meinicke s reaction (G Battistini) —*Riforma med*, Aug 17, '35, p 1244

Hinton test value in 3000 cases (L Hollander *et al*) —*Urol & Cut Rev*, Sept '35 p 617

Arsphenamine Compounds —Blindness after neoarsphenamine (F Juler) —*B J Ophth*, Sept '35, p 526

Arsenical hepatitis treatment with sodium dehydrocholate (Appel and Jankelson) —*Arch D & S*, Sept '35 p 422

Acetarsol (stovarsol) in treatment of congenital syphilis (H S Mitchell) —*C M A J*, Oct '35, p 377

Stovarsol treatment (M Oppenheim) —*Indian J Ven Dis*, June '35, p 89

Bismuth Therapy —In treatment of syphilis (R K Sen) —*Indian J Ven Dis*, June '35, p 111

Modified composition of iodobismitol (P J Hanzlik *et al*) —*Arch D & S*, Aug '35, p 284

Mercury.—Mercury inunctions (T Sollmann *et al*) —*Arch D & S*, Aug '35, p 242

Excretion of mercury after intramuscular and intravenous injections (T Sollmann *et al*) —*Arch D & S*, July '35, p 1

Neurosyphilis —Exclusion of neurosyphilis by Hinton test (J L Grund) —*Arch D & S*, Oct '35, p 569

Tryparsamide in dementia paralytica (Solomon and Epstein) —*Arch Neur & Psychiat*, June '35 p 1216

Therapeutic malaria some results (G de M Rudolf) —*Med Press* Sept 18, '35, p 255

Pyrexial treatment of mental and nervous disorders (E J T Thompson) —*Med Press*, Aug 7, '35, p 119

General paralysis treatment with ape malaria (Rooyen and Pile) —*B M J*, Oct 12, 35, p 662, (Edit) *Ibid*, p 672

Pyrotherapy in dementia praecox (D Menzies) —*Lancet*, Nov 2 '35, p 994

Rationale of malaria therapy in cerebrospinal syphilis (E C Menzies) —*C M A J*, Nov '35, p 504

TETANUS

Since the introduction of antitoxin the mortality from tetanus has been reduced to little more than half At the same time, it is recognized that patients may succumb to the symptoms alone and that it is desirable to keep the spasms well under control, and for this purpose a powerful sedative is indicated Avertin is much in favour 0 08 to 0 10 gm per kilo of body-weight is given per rectum, followed by smaller doses from time to time before the effect wears off A drug that seems to be increasing in favour is curare, or its alkaloid curarine, but the difficulty of obtaining samples of known potency must interfere with its usefulness

Antitoxin treatment, prophylactic and therapeutic, is the subject of several articles, one of which recommends the following dosage after the usual tests for sensitivity on admission, 20,000 units intravenously, the same amount intramuscularly, and 2000-5000 units injected locally round the wound, 20,000 units intramuscularly on the second and third days, 10 000 units intramuscularly seven days after the last dose It is shown by some workers that antitoxin disappears from the blood rapidly at first and more slowly later, seven days after injection about 10 units per ml and after fourteen days 3-5 units per ml remains in the blood They recommend as routine treatment a single intravenous dose of 200,000 units as early as possible, followed by thorough treatment of the wound, a liberal diet, and avertin (or curare) to control the spasms Persistence of antitoxin in the blood for one or two years has also been recorded The references given below will enable readers to amplify this information if desired

Present status of treatment (Miller and Rogers) —*J A M A*, Jan 19, '35 p 186

Editorial on treatment —*Lancet*, Aug 3 '35, p 256

Analysis of 185 cases at New Orleans Hospital (Boyce and McFettridge).—*New Orleans M. & S.J.*, June '35, p. 825.

Tetanus in a child aged 23 months, successfully treated with anti-tetanus serum (J. D. Spillane).—*Lancet*, Aug. 3, '35, p. 249.

Treatment, with observations on the fate of injected antitoxin (Cole and Spooner).—*Q.J.M.*, July '35, p. 295.

Persistence of antitoxin in man following active immunization (Sneath and Kerslake).—*B.M.J.*, Aug. 17, '35, p. 290.

Prognosis of tetanus (L. Cole).—*Lancet*, Oct. 26, '35, p. 957.

Avertin a valuable auxiliary measure (H. S. Mitchell).—*C.M.A.J.*, Apr. '35, p. 415 (P. Nov. 358).

Use of avertin to control convulsions (A. W. Fawcett).—*B.M.J.*, June 8, '35, p. 1171 (P. Nov. 358).

Case treated with avertin and antiserum (C. Berman).—*S.Af.M.J.*, May 11, '35, p. 315.

Treatment with continuous avertin anaesthesia (L. Cole).—*Lancet*, Aug. 3, '35, p. 246.

Case successfully treated with curarine (J. S. Mitchell).—*Lancet*, Feb. 2, '35, p. 262 (P. Nov. 358).

Evipan intravenously in symptomatic treatment of traumatic tetanus (P. Walzel).—*S.m.W.*, Jan. '35, p. 80.

TUBERCULOSIS.

The literature on tuberculosis, in so far as it relates to diagnosis and treatment, was reviewed in our issue of July last. In that review much valuable work was recorded, but little that was really new. The tuberculin test has been further studied: the Mantoux test seems to be most in favour. A new and promising form of tuberculin for testing purposes, the purified protein derivative ('Tuberculin P.P.D.'), has been introduced in tablet form, which has the great advantage of accuracy of dosage.

Gerson's salt-free diet is still attracting attention, but to a less degree. Tuberculin treatment is still the subject of controversy. The value of BCG vaccine is being studied further. A preparation called 'nordalin,' described as a sulphoguaiacolic acid precipitate of the plasma of immunized animals, has been favourably reported on by several workers. As regards drug treatment, gold compounds still hold the field: sanocrysin is popular, and several organic compounds of gold show promise of usefulness.

Abstract review: general; diagnosis; tuberculin tests; tuberculin P.P.D.; Vernes test; prognosis; dietetic treatment; tuberculin and vaccines; BCG vaccine; nordalin; gold therapy; miscellaneous remedies.—PRESCR, July '35, p. 225.

Recent References.

Varieties of tubercle bacillus (Edit.).—*Lancet*, June 22, '35, p. 1454.

Family tuberculosis due to bovine bacilli (Griffith and Munro).—*B.M.J.*, July 27, '35, p. 147.

Significance of pyrexia in chronic pulmonary tuberculosis (M Myers) —*B M J*, Aug 10, '35, p 250

Tuberculin allergy in acute infectious diseases a study of the intra cutaneous test (J S Westwater) —*Q J M*, July '35, p 203

Tuberculin treatment of cutaneous tuberculosis (H S Brunell Jones) —*B M J*, June 15, '35, p 1212

Experiments relative to vaccination against tuberculosis with BCG (B J Clawson) —*Arch Pathol*, Sept '35, p 343

Committee to study use of BCG (Paris letter) —*J A M A*, July 27, '35, p 293

BCG vaccination in Sweden (Edit) —*Lancet*, June 29 '35, p 1512

Nordalin treatment (S G Tippett) —*Med World*, Oct 18 '35, p 226

Gold treatment (Peters and Short) —*Lancet*, July 6, '35 p 11

Sanocrysin in pulmonary tuberculosis review of results in different countries (G G Kayne) —*P R S M*, Sept '35, p 1463

Treatment of pulmonary tuberculosis by ultraviolet radiation (Coulter and Carter) —*J A M A*, July 20, '35, p 171

Light therapy and x ray therapy (E Mayer) —*J A M A*, Nov 16, '35, p 1599

TYPHOID FEVER.

The only point in the treatment of typhoid fever that has emerged during the year is the trial of a new antityphoid serum prepared at the Lister Institute The serum is unconcentrated and contains antibodies to both the 'O' and the 'Vi' antigens to a titre of 1 in 40,000 and 1 in 400 respectively The presence of both these antibodies is regarded as essential to its therapeutic efficacy This serum has been tried by two workers independently with encouraging results

Clinical trials with a new antityphoid serum (A Felix) —*Lancet*, Apr 6, '35, p 799

Clinical trials with a new antityphoid serum (C J McSweeney) —*Lancet* May 11, '35, p 1095 (P Sept. 285)

UNDULANT FEVER

Nothing of real importance emerges from the literature on undulant fever during the past year The incidence of the disease in this country remains low, and little opportunity is offered for its study The value of the agglutination test, except with a high titre, has been called in question Treatment continues to be mainly symptomatic, though both vaccines and serums have been advocated one serum, described by Canadian workers, seems to have given particularly good results

Recent views on the *Brucella* group (E M Robinson) —*S Af M J*, Sept 28, '35, p 645

Undulant fever in Scotland (C P Beattie *et al*) —*Lancet*, June 22 '35, p 1427

Does positive agglutination reaction prove the presence of *Br. abortus* infection (W. Hauptmann)?—*Med. Klin.*, Aug. 30, '35, p. 1174.

The intradermal test: reactions in healthy and infected persons (Favorite and Culp).—*J.L.C.M.*, Feb. '35, p. 522.

Difficulties in diagnosis and treatment (H. J. Harris).—*N.Y.St.J.M.*, Dec. 1, '34, p. 1017.

Treatment of undulant fever (J. E. Debono)—*Lancet*, Feb. 16, '35, p. 374.

Treatment of acute and chronic undulant fever: 100 cases in seven years (F. E. Angle).—*J.A.M.A.*, Sept. 21, '35, p. 939.

Antiabortus serum (C. A. Mitchell *et al.*).—*Canad. Pub. Health J.*, May '35, p. 209.

Serum and vaccine therapy of undulant fever (Hilgerman).—*M.m.W.*, Jan. 17, '35, p. 98.

Treatment by protein shock (Beaumont and Page).—*Lancet*, Oct. 26, '35, p. 940.

Septicaemia due to *Brucella abortus* following operation (Potter and Harburn).—*B.M.J.*, May 25, '35, p. 1068.

WHOOPING-COUGH.

As mentioned in this place last year, the most important recent development in the therapy of whooping-cough has been a revival of interest in vaccine therapy. Vaccines for pertussis have been on trial for many years, but hitherto no conclusive evidence of their efficacy has been available. During 1935 a number of articles on vaccine prophylaxis and treatment have been published. Sauer (U.S.A.) used as a prophylactic a vaccine differing from all other pertussis vaccines in being made every few months from recently isolated haemolytic strains of the Bordet-Gengou bacillus. This was used on a large number of infants and young children, with strong evidence of immunity as compared with controls. Sauer says that immunity takes about four months to develop, but it lasts probably for years. If the vaccine is given less than four months before exposure it appears to be useless as a preventive. Sauer's vaccine, as originally devised at the Northwestern University Medical School, Illinois, is prepared and sold by Eli Lilly and Parke, Davis & Co. The Council on Pharmacy and Chemistry, A.M.A., has decided to reserve judgment pending further evidence of its value. Paterson and colleagues (London), in a recent article, report trials with Sauer's vaccine (Lilly), and find that it can be used as a skin test. By intradermal injection it can be used to diagnose whooping-cough in an early stage or to pick out those children who are susceptible to the disease. These workers have used convalescent serum with benefit in the prophylaxis but with doubtful benefit in the treatment of pertussis.

Considerable work has been done in Europe on vaccine therapy. Kaupe (Bonn) reports trials with a vaccine made in Germany (Behring), a strong preparation, of which three injections representing respectively 4000, 6000, and 8000 million organisms are said to

be sufficient to produce immunity Workers in other European countries have also reported trials Finally Blaubaum (Melbourne) reports successful treatment of a number of cases with a pure pertussis vaccine prepared in the Commonwealth Serum Laboratories Large doses are necessary—100 million working up to 2000 million in infants according to the severity of the case, while older children receive 1000 million up to 3000 or even 5000 million Early treatment is more effective, and the vaccine makes symptoms less severe and renders the advent of complications less probable

Many drugs have been recommended for treatment Gold tribromide is warmly supported by one worker (Epstein), who for some years has been publishing reports of its successful use, though we have been unable to find any confirmation of its value by others Pentnucleotide has been tried, and painting the aural passages with an analgesic solution was enthusiastically advocated by Stephens (Swansea) in our issue of July last

Serological diagnosis and specific treatment (M Gundel *et al*)—*Ztschr f Kinderh*, 1935, lvii, 89

Bacteriological diagnosis (Silverthorne and Fraser)—*C.M.A J*, Apr '35, p 367

Diagnostic significance of blood counts (Begg and Coveney)—*Lancet*, Nov 16, '35, p 1113

Whooping-cough without the whoop clinical diagnosis (P R Evans)—*B M J*, Dec 8, '34, p 1043

Treatment general (W T Benson)—*B M J*, Mar 30, '35, p 657

Adrenal gland and serotherapy in treatment (O Barbour)—*Arch Pediat*, Mar '35, p 143

Gold tribromide 100 cases with 50 controls (J Epstein)—*Med Record* Jan 16, '35, p 99

Syringing ears with boric acid solution and painting with procaine solution (G A Stephens)—PRESCR, July '35, p 224

Pentnucleotide treatment (J G M Bullows *et al*)—*Am J Dis Ch*, Jan '35, p 91

Convalescent blood injections 58 cases (W L Bradford)—*Am J Dis Ch*, Oct '35, p 919

Treatment with active undenatured antigen (Stallings and Nichols)—*Am J Dis Ch*, Dec '34, p 1183

Experimental supersensitiveness to undenatured *H pertussis* protein (Miller and Browne)—*Proc Soc Exper Biol & Med*, Dec '34, p 449

Immunization against whooping-cough (L W Sauer)—*Am J.Dis Ch*, Jan '35, p 69, *N Y St J M*, Aug 15, '35, p 821

Report on Sauer's vaccine by Council on Pharmacy and Chemistry, A M.A—*J A M A*, Mar 9, '35, p 834

Experience with vaccine treatment (W Kaupe)—*Med Klin*, Jan 18, '35, p 79

Pertussis vaccine (I Blaubaum)—*M J Australia*, Apr 6, '35, p 432

Vaccine therapy (W Bayer)—*Klin Wschr*, Mar 2, '35, p 301

Control of whooping-cough with serum and vaccine uses of a new skin test (D Paterson *et al*)—*Lancet*, Aug 17, '35, p 361—(Edit) *Ibid*, p 377

THERAPEUTIC ABSTRACTS.

Calcium in Tropical Diseases.—BEREGOFF (Montreal) finds from examination of a large number of persons who have lived in the tropics that the calcium content of the blood in such persons is invariably below normal This is particularly noticeable in persons suffering from tropical skin troubles In such cases calcium gluconate in large doses improves the condition and helps the healing process Most of the patients received 10 ml of a 10 per cent solution, intravenously or intramuscularly, every other day for six or eight weeks

BEREGOFF, P Calcium therapy in tropical diseases *Canad Med Assoc J*, 1935 Feb, 177-178

Insulin in Toxic Diphtheria.—The significance of sugar tolerance curves and the value of insulin in toxic diphtheria have been studied by BEGG and HARRIES (London) Antitoxin intravenously and intramuscularly and dextrose intravenously and by mouth are the accepted basis of treatment The response of the body to dextrose is constantly abnormal and results in higher blood-sugar findings the degree of variation is an index to the severity of the attack and a guide to the progress of the disease A close association seems to exist between abnormalities in tolerance curves and involvements of the cardiovascular mechanism Insulin does not appear to change the character of the abnormal curves, nor does it influence the course of the disease

BEGG, N D with a note by HARRIES E H R Toxic diphtheria the significance of sugar tolerance curves and the value of insulin *Lancet* 1935 March 2, 480-485

Cannabis Indica Intoxication.—BAKER-BATES (Liverpool) reports a rather curious case A young man sowed ordinary hemp seeds in his garden, and when the plants had grown up he removed the leaves, dried them, and made them into cigarettes On smoking these he noticed mild symptoms of intoxication—loss of sense of time and space, vivid hallucinations, and subsequent drowsiness Incredulous about his experiences, his fiancee smoked (and inhaled) a portion of a cigarette, and soon developed very pronounced symptoms of intoxication—typically those of cannabis—which lasted for nine hours, but eventually passed off leaving only a severe headache It is suggested that the hot summer caused the plants to develop the active resin, usually found only in plants grown in India

BAKER BATES, E T A case of cannabis indica intoxication *Lancet*, 1935, Apr 6, 811

Acidosis in Children.—Discussing so-called acidosis in children, PATERSON (London) remarks that the term 'acidosis' is usually applied to the formation of ketone bodies in the blood and urine, the symptoms being fever, vomiting, and diarrhoea Such a diagnosis is incorrect · it is merely a clinical description and does not elucidate the underlying condition, which is usually infective and not dietetic in origin The shift of the *pH* of the blood to the acid side induced

by mineral acids—biochemical acidosis—is not what is usually meant by the term as used clinically Search should be made for the source of infection, usually naso-pharyngeal, and this should be treated Prevention depends on educating the mother to be on the alert for the first signs of liver infection, which gives rise to this systematic vomiting

PATERSON D So called acidosis attacks a plea for more accurate diagnosis *Lancet*, 1935 Apr 20 917 919

Uric Acid and Gout.—The pathogenesis of gout is discussed at some length by LUCKE (Gottingen) The disease, he says, is characterized by typically recurring attacks accompanied by certain disturbances in the secretion of uric acid Prior to the attack the amount of uric acid in the urine is considerably decreased, during the attack it is increased, and after the attack it again decreases As a result, the kidney shows anatomical changes, taking on a condition similar to that found in nephrosclerosis Hyperuraemia occurs immediately before an attack of gout, and becomes strongly marked as attacks continue In slight attacks the blood-urea is between 4 and 6 mg per cent, while in typical attacks it may rise to 8 mg per cent, or even higher when the kidney becomes nephrosclerotic Another typical symptom of gout is the crystallization of urates in certain tissues Some authorities regard gout as an allergic disease brought on by certain kinds of wine or food, while others regard the condition as the result of changes in the vegetative nervous system These explanations, however, take no cognizance of purine, which has been shown to be the most important factor in the development of gout

LUCKE H Die Rolle der Harnsäure bei der Gicht *Dtsch med Wschr*, 1934 Nov 23 1783-1786

Serum Treatment of Lobar Pneumonia.—JOHNSTON (Edinburgh) states that beyond the third or fourth day of illness serum offers no great advantage in the treatment of lobar pneumonia, but in the early stages it helps in overcoming the bacterial infection Felton's 'serum' (which is not strictly a serum but is more accurately described as a concentrated pneumococcal antibody solution) offers a therapeutic measure which under suitable conditions appreciably lowers the mortality As yet it cannot be adopted universally, as its administration requires experience and technical skill in typing, while its cost is high In its preparation standard antipneumococcal serum is first incubated with sodium sulphate, when a precipitate forms which is filtered off and dialysed in running water for five days The contents of the dialysing sac are adjusted to *p*H 4 6 to 4 8 when a second precipitate forms which is removed The clear supernatant fluid is adjusted to *p*H 6 8 and diluted with water, when a white precipitate forms which contains all the protective substance of the original serum and is practically free from protein shock factors This precipitate is dissolved in sodium chloride solution

JOHNSTON J M Lobar pneumonia and its serological treatment. *Edinburgh Med J* 1935 May 265 279

Potassium Permanganate as an Antidote —It is pointed out by HATCHER (New York) that certain misapprehensions exist regarding the antidotal action of potassium permanganate Its field of usefulness is distinct but limited it should be remembered that even fairly dilute solutions are irritant, and that a large dose may cause death Potassium permanganate may be given orally in concentrations varying from 1 2000 to 1 5000, and 1 5000 may be used for washing the stomach, in poisoning by aconitine, amidopyrine, morphine, phenazone, picrotoxin, and strychnine It will not destroy all the poison, and its use should be followed by evacuation of the stomach It is useless as an antidote in poisoning by atropine, cocaine, phosphorus, and by most of the synthetic hypnotics There is no justification for the intravenous, subcutaneous, or intramuscular injection of potassium permanganate for the destruction of any poison in the circulation

HATCHER R A The antidotal action of potassium permanganate *J.A.M.A.*, 1935 Aug 17 502 504

Liver Therapy in Smallpox.—NAIR (Vizagapatam) reports a series of twenty-eight cases of smallpox treated with intramuscular injections of liver extract He finds that this treatment modifies the course of the disease, shortens its duration, aborts the eruption, and avoids consequent disfiguration from pitting The systemic disturbances soon disappear and the patient goes through the attack with comparative comfort None of the cases showed itching at the time of incrustation, nor developed boils and subcutaneous abscesses, secondary septic fever, toxic rash, or phlebitis and thrombosis, the usual complications of untreated cases of smallpox Two brands of liver extract were employed—campolon (Bayer) and an extract made in Calcutta—and both gave equally good results

NAIR V G Treatment of smallpox with liver *J Indian Med Assoc* 1935' July 488 496

Haverhill Fever (Erythema Arthriticum Epidemicum).—This disease, apparently a new clinical entity first recognized in Haverhill, Mass , is described by PLACE and SUTTON It is characterized by an abrupt onset, often with a chill, a rubella like or morbilliform eruption chiefly on the extremities, with a tendency towards haemorrhage into the lesions, and an inflammation of the joints with marked pain and tenderness The disease occurred as a localized epidemic and was evidently spread through the milk supply An organism, *Haverillia multiformis*, is believed to be the cause , it was found in the blood in most of the cases Cutaneous reactions to killed suspensions were present in 83 per cent of the patients tested in convalescence Although crippling may remain for a time, recovery usually occurs in one or two months , a small number of patients have persistent joint symptoms No fatalities are reported

PLACE E H and SUTTON L E Erythema arthriticum epidemicum (Haverhill fever) *Arch Int Med*, 1934 Nov , 659 684

NEW REMEDIAL AGENTS.

Cancer: A New Treatment.

THE announcement made recently by HENRY C CONNELL, of Queen's University, Kingston, Ontario, that he had discovered a new treatment for cancer has aroused considerable interest on both sides of the Atlantic Connell's paper is purely preliminary, and he is very cautious in his conclusions—two features which at least call for sympathetic consideration of his statements In his studies on the cataractous lens, Connell, who is an eye specialist, noted the action of a certain proteolytic microorganism in producing an enzyme having a specific action on lens protein This led to the idea that he might be able in a similar manner to produce an enzyme that would act on cancer cells, and such he claims to have succeeded in doing Experiments *in vitro* showed that human breast carcinoma tissue, inoculated with *B histolyticus* (*Clostridium histolyticum*) in pure culture, was in a few days completely digested by the enzymes secreted by the bacillus Further experiments upon mice, in which this enzyme solution—which he terms 'ensol'—was injected intramuscularly, showed that in a short time the tumour cells (mouse carcinoma) underwent various degrees of destruction Not being an expert in this particular work, Connell referred the matter to the Imperial Cancer Research Institute, London, and a recent communication from GYE of that institution states that ensols made according to Connell's directions were without effect on mouse tumours

Meanwhile as several cases of carcinoma were under his care for eye conditions, Connell decided to try the effect of an autogenous ensol on these Intramuscular injection caused no inflammatory or other systemic reaction, and the immediate effects are described as 'remarkable and quite unlike anything previously observed' Thirty cases are described, and while it is admitted that in some the treatment elicited no response, those that did respond showed consistent improvement

The following is Connell's formula for the preparation of 'ensol' About 10 gm of malignant tissue is removed at operation under sterile conditions, and dissected free from normal tissue One gramme of this is placed in a test-tube with 10 ml of normal saline solution, this is inoculated with pure culture of *Cl histolyticum* and incubated at 37 5° C under anaerobic conditions for from four to six days, or until the fluid contents have settled out The contents of the tube are then centrifuged and the supernatant fluid is filtered through a Berkefeld candle Viability tests on this filtrate are made, and if it is found to be sterile the enzyme solution is ready for use

Treatment of cancer by proteolytic enzymes is not a new idea it was suggested twenty-nine years ago by an Edinburgh worker and was mentioned in these pages at the time (PRESCRIBER, 1907, Feb, 70) Then the subject was stated to be in the experimental stage, and it

does not seem ever to have gone any further. Previous experience leads one to treat such announcements with a cautious scepticism; at the same time it is only fair to grant any worker a fair hearing, especially in so vital a matter as the treatment of cancer.

CONNELL, H. C. The study and treatment of cancer by proteolytic enzymes: a preliminary report *Canad. Med Assoc. J.*, 1935, Oct, 364-370
GYE, W. E Treatment of cancer by proteolytic enzymes (corresp.). *B.M.J.*, 1935, Oct. 19, 760

New Drugs and Preparations.

[Under this heading are given brief notices of new non-secret products as they appear on the market or are mentioned in medical literature. The notes are intended for reference only, and must not be taken to imply anything in the nature of a recommendation. In most cases the information is derived wholly or mainly from makers' advertisements]

Cerocol.—Colloidal cerium oxalate, a form readily absorbed. Cerium oxalate has a sedative action and is an old-established remedy for vomiting of all kinds, but its extreme insolubility has caused it to be abandoned. It is claimed for cerocol that it is readily absorbed and acts promptly, and that it is non-toxic and non-irritating Tablets, 0 05 gm. (¾ grain); dose one or two, allowed to disintegrate on the tongue. (Coates & Cooper Ltd., London.)

Ensol.—A solution containing enzymes and said to be specific for cancer. Prepared from human cancer tissue inoculated with *B. histolyticus*. Described by H. C. Connell.—*Canad. Med. Assoc. J.*, Oct. '35, p. 364.

Ergobasine.—A water-soluble alkaloid of ergot of rye, isolated by Stoll and Burckhardt. It is stated to be analogous to, but distinct from Dudley and Moir's ergometrine.—*Bull. Sc. Pharmacol.*, May 1935.

Ergometrinine.—An alkaloid of ergot, stated by Smith and Timmis (*Nature*, Aug. 17, '35, p. 259) to have been obtained during the process of manufacture of ergometrine.

Ergotocin.—A crystalline principle isolated from ergot by F. L. Adair *et al.* (Chicago), and said by them to be responsible for most, if not all, of the oxytocic effect of the drug.—*Amer. J. Obst. & Gynec.*, Oct. '35, p. 466.

Estoform.—Orthoformic ester, $HC:(OC_2H_5)_3$, 10 per cent., combined with extracts of wild cherry and senega in a medium of glycerin and spirit. Antispasmodic, recommended in coughs, bronchitis, and asthma. Dose, 2 to 6 teaspoonfuls well diluted with water. (Crookes Labs, London.)

Hydronal.—A preparation of aluminium hydroxide for relief of hyperacidity in gastric ulcer, etc. It forms a gel which neutralizes excess of acid and furnishes a protective coating for the mucous membrane. Tablets, 7½ grains. Dose, one to three before meals, according to the severity of the symptoms; to be chewed before swallowing. (Bayer Products Ltd., London.)

Lettocine.—The name given to a new alkaloid isolated by F. H. Peacock and J. C. Chowdhury from the bark of *Holarrhena antidysenterica*, a tertiary base with no hydroxyl groups. Its therapeutic action does not seem to have been studied.—*J. Chem. Soc.*, 1935, June, 734-735.

Lovibond Limitester —A simple form of comparator for application of the phosphatase test for the detection of raw or insufficiently heated milk in pasteurized milk The absence of phosphatase indicates that the milk has been adequately heated A free booklet describing the test is offered to those interested (British Drug Houses Ltd London)

Mesodine —A compound of an acridine dye with arsenic in organic combination recommended in the treatment of female gonorrhoea In 1 per cent aqueous solution Known on the Continent as *Flavadin* (Bayer Products Ltd London)

Novurit —A 10 per cent aqueous solution of an organic salt of mercury ($C_{10}H_{28}O_6NHgNa$) with 5 per cent theophylline Recommended by Rissmann (*Münch med Woch* July 5 35 p 1074) as a diuretic Contains no free mercury ions (Henning Berlin)

Peptalac —A predigested milk diet in powder form requiring only the addition of water to form a peptonized food (Cow & Gate Ltd)

Phospho-Soda —A pure concentrated solution of sodium dihydrogen phosphate (sodii phosphas acidus B P) containing 60 grains in each fluid drachm Recommended as a remedy for constipation and for affections of the liver and gall bladder Dose one to four teaspoonfuls (Anglo French Drug Co Ltd London)

Picochrome —A urinary antiseptic described as a derivative of ortho cresyl Said by A Ravich to act equally well in acid and alkaline urines and to be destructive of coliform bacilli as well as cocci It colours the urine red —*Med Record* Apr 3 35 p 343

Pitantrin —A preparation of the anterior pituitary like sex hormone for hypodermic administration in vials of 10 ml containing 100 rat units (G W Carnrick Co Brooks & Warburton Ltd London)

Prontosil Prontosil S —Two synthetic compounds said to be effective against infections due to haemolytic streptococci Can be given either by mouth or subcutaneously

Rossium —A synthetic compound described as diphenyl methyl pyrazolonyl (antipyrin is phenyl dimethyl pyrazolone) recommended for the treatment of morphine and opium addiction Given in doses of 1 0 gm (2 capsules) the total number of capsules per day being one tenth of the body weight in pounds Capsules 0 5 gm (Medico Chem Corpn New York)

Sodium Mandelate —The sodium salt of mandelic acid a convenient way of administering that acid in urinary infections (see PRESCRIBER 1935 Sept 288 289) A white powder soluble in water Dose 3 5 gm four times daily after meals (Boots Pure Drug Co Ltd Nottingham)

Soneryl —A barbituric acid derivative *n* butylethylbarbituric acid recommended as a hypnotic and analgesic Average adult dose 3 grains maximum 9 grains daily Tablets 1½ grain ampoules 1½ grain in 2 ml (May & Baker Ltd Dagenham)

Targesin —A colloidal compound of acetyltannin with silver albumin containing 6 per cent of silver Described by W Krause (*Münch med Wschr* Aug 9 35 p 1285) as a remedy for gastro intestinal troubles (Goedecke & Co Berlin)

REVIEWS OF BOOKS.

Prescription Writing and Formulary · The Art of Prescribing By Charles Solomon, M D , Long Island College of Medicine Pp 351 (Lippincott 21s)

With that thoroughness characteristic of American authors Dr Solomon has endeavoured to cover the entire subject of prescription writing, and he has undoubtedly succeeded, though much of what he says is very elementary His chapters on the prescription are particularly thorough, and his list of actual prescriptions occupies nearly half the book Unfortunately for students in this country the book is written entirely from the viewpoint of the United States the U S P is the standard, the Harrison Law takes the place of our Dangerous Drugs Act, prices of expensive drugs are quoted in dollars and cents, and the pint is only 16 ounces The chapter on Incompatibility is obviously based on Stephenson's work, and a fuller acknowledgement might have been made than mere mention in the bibliography at the end of the book On page 43 we are told that ' isotonic solutions have the same density as the blood —0 9 per cent '—per cent of what ? Apart from these little discrepancies, which can be remedied in future editions, one cannot but admire the extreme thoroughness with which the subject is treated, and the book should prove helpful to students, particularly in America

Royat Treatment in Cardiovascular Disease By Pierre Noel Deschamps, M D Paris Pp 108 (Baillière, Tindall & Cox 5s)

This small brochure brings to the notice of physicians the advantages of the waters of Royat The general action of thermal waters containing CO_2 is discussed, especially their local action on the skin and their effect after absorption into the blood The chief effects are superficial vascular dilatation and lowering of blood-pressure, with what is described as a sedation of vagosympathetic excitability The application of these effects to conditions such as hypertension, cardiac insufficiency, and angina pectoris is described, and the book concludes with remarks on details of treatment, diet, and hygiene J O

Physical Signs in Clinical Surgery By Hamilton Bailey, F R C S Fifth Edition Pp 287 (Wright, Bristol 21s)

Five editions besides extra impressions within the short space of seven years is surely recommendation enough for any book The chief recommendation of this excellent manual, however, is the book itself It was primarily written to prove the immense value of the history and physical examination of the case in coming to a diagnosis, and the reader will be inclined to agree that this thesis has been amply proved Bailey quotes Wade in saying ' The wards are the greatest of all research laboratories,' and certainly no worker in the wards, especially should he be a novitiate, should be without this book

The present edition does not differ greatly from its predecessor, but there has been a thorough revision of the text and several new illustrations have been added There is little that one can pick out for mention, so uniformly good are the chapters That on the breast is specially well illustrated and gives the beginner a good idea of breast examination and

Under the title of MIND AND VISION, Dr R. S Agrawal, Delhi, has published a small book of 180 pages describing his treatment of imperfect sight without glasses His thesis is that by proper exercise of the eye muscles the circulation is stimulated and the optic nerve is strengthened by a fresh supply of blood His methods are based on those of Mr Bates of New York, and are adapted for use in India, but if they are of any value they might well be adopted anywhere The book is published by Dr Agrawal's Eye Institute, Delhi, at Rs 4

The latest of Professor Weekley's excursions into wordlore is called SOMETHING ABOUT WORDS (Murray, 5s) and consists of lectures he has delivered and articles he has written during the last few years All eleven chapters are delightful reading, though we might mention those on the Future of English, on Walter Scott's contributions to English, and on Anglo-Indian English as perhaps the most enjoyable The idiom used by Babbitt is described as 'English in an advanced state of decomposition' We are told that 'two demons are fighting for the soul of our language, the broadcasting demon of standardization and the cinema demon of vulgarity,' and our author fears that democracy will choose the broad way that leadeth to destruction It seems that Scott has done more than anyone to revive old Shakespearean and other obsolete words and to give them currency in modern language The Anglo Indian contributions to our language are many of them unexpected, even to one who, like the reviewer, can claim to be fairly familiar with them And the story of the old lady who had always thought Dan and Beer Sheba were man and wife, like Sodom and Gomorrah, is an example of the touches of humour that abound in this delightful book

THE BLACK EYE is the title of the latest work of Dr H O Mavor, known to the play going public as James Bridie (Constable 2s 6d), and is another of our author's little jokes George Windlestraw appears in the first scene with a black eye, the remainder of the two act play explains how he got it, though the injury itself is a very minor part of the story The moral—if moral it can be called—is in George's own words 'if you chance your arm and let yourself go blind into the future, you've got a sort of sixth sense or something that sees you through It happened in George's case, but he would be a very foolish man who trusted entirely to this 'sixth sense or something' Still it makes a good play, at least to read, we have not yet had an opportunity of seeing it acted

Diaries for 1936.

BAYER PRODUCTS LTD.—This firm's diary is on lines very similar to the 1935 issue In addition to the usual diary and cash pages is a complete list with prices of the Bayer products and an amount of general information. The book is compact pocket size neatly bound and well printed

WILLIAM R WARNER & CO LTD.—The diary calendar issued by this firm also follows the lines of last year It is designed for desk use and contains numerous therapeutic and miscellaneous notes of an interesting character

Both these publications are issued free to the medical profession Any physician who has not received a copy should write to the publishers whose addresses will be found in our advertisement pages

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The Prescriber.

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The Late King George V.

As we go to press comes the sad news of the death of our beloved King. We join with the nation in expressing our profound sorrow and our sympathy with the Queen Mother and the rest of the Royal Family. To the new King we extend our wishes for a long and prosperous reign.

THE ANAEMIAS.

THE close attention accorded in recent years to the anaemias has already resulted in very considerable additions to our knowledge of this group of diseases. Improved methods of blood examination and extensive research into the nature of these conditions have led to a better knowledge of underlying causes and to the introduction of improved and reliable therapeutic methods. The literature is still voluminous, and its presentation in abstract form occupies the greater part of the present issue. Careful study of the succeeding pages will show that while much yet remains to be discovered, light has already been shed on many of the dark places.

Classification of the anaemias is still a matter of controversy, and it will remain so until certain aetiological factors are better understood. Meanwhile the practice of coining a new name for every variety that seems to differ from what has gone before is to be deprecated. Diagnosis, it is now realized, depends mainly on an accurate blood examination, and it is being further recognized that treatment should be controlled by such examinations.

Pernicious anaemia is still the most widely studied member of the group. The researches of Castle and

co-workers point to its being a deficiency disease conditioned by the lack of a specific intrinsic factor present in normal gastric juice, its function being to interact with an extrinsic factor in the food. Quite recently Meulengracht has shown that this intrinsic factor exists only in the pyloric glands: this may explain the occasional failure of treatment by desiccated stomach. Attempts to isolate the haematopoietic principle of liver extract have met with a certain degree of success, and an accurate method of biological assay of this extract seems also to be within reach.

Next to pernicious anaemia, the greatest amount of study has been given to the nutritional anaemia of infancy. The anaemias of infancy are many, but by far the most common is that due to deficiency of iron. Infants receive little, if any, iron from their milk: they rely on the normal supply stored in the liver during the later months of foetal life. When for any reason this store is insufficient the child will most likely develop anaemia during its first few months of life. Routine administration of small doses of iron and ammonium citrate to all infants during the first twelve months of life will effectually prevent such an occurrence.

Other types of anaemia have received attention: the hypochromic anaemia of adults is now fairly well understood and little has been added to what is already known. Aplastic anaemia, splenic anaemia, the anaemia of scurvy, as well as several other types have all contributed to the general study. The condition known as agranulocytosis or agranulocytic angina has claimed particular attention, its supposed relation to certain drugs and its successful treatment with pentose nucleotide being the subject of numerous communications. A special article dealing with this condition and with acute leukaemia has been contributed by Dr J. D. Comrie, while the latest literature on agranulocytosis is reviewed at the end of the article dealing with the anaemias.

The foregoing affords a very rough indication of the contents of the present issue. The subject is of great interest and importance in medical practice, and we commend the present issue to our readers with confidence.

ORIGINAL COMMUNICATION.

Some Rarer Conditions of the Blood.

By JOHN D. COMRIE, M.A., B.Sc., M.D., F.R.C.P.

I. Agranulocytosis.

FOR several decades it has been well known that certain drugs, such as benzol, administered to cases of myeloid leukaemia, produced marked decrease in the number of white blood cells, and this form of treatment for a time had a considerable reputation. It was also recognized that leucopenic cases of acute leukaemia were liable to necrotic ulcerations and infectious complications. In 1922 attention was first drawn by Schultz[1] to the fact that a similar reduction of the granular leucocytes might occur in febrile cases where previously there had been no leukaemia, and he suggested as a cause of this condition invasion by some hitherto unknown micro-organisms. In the succeeding thirteen years, more than 500 cases have been recorded in which this reduction or disappearance of the granular leucocytes took place, usually with a fatal result, and the syndrome has received the name of agranulocytosis or agranulocytic angina. The condition is characterized by a marked reduction of all the white corpuscles to a count of about 1000 or even a few hundreds. This reduction especially affects the granulocytes (polymorphonuclear leucocytes) which may be diminished from 70 per cent. of the total white cells to 5 per cent., or may even be completely absent. In fatal cases, an examination of the bone-marrow shows corresponding changes, the myelocytes either being greatly diminished, or in other cases immature forms being abundant to the exclusion of the more mature granulocytes. In all cases the patient is seriously ill with raised temperature and necrotic or ulcerative lesions of mucous membranes, most frequently in the mouth and pharynx, but sometimes also in other parts such as the rectum.

The disease begins acutely with rigors, prostration, pains in the limbs, and particularly sore throat. The temperature is high, varying between 100° and 105° F., and there is an exudation on the tonsils and pharynx. This condition corresponds to what used to be called

'putrid sore throat,' and many cases previously recorded as cancrum oris were probably examples of the same condition. The cervical glands become enlarged and the throat oedematous and indurated so that swallowing may become difficult. The infective and gangrenous process may later spread down the alimentary canal to affect the intestines, or in some cases the inflammation from the first is situated in the colon and rectum.

The patient is pale but there is no great degree of anaemia, the striking feature when the blood is examined being the reduction of the white blood corpuscles. Throat swabs show a variety of organisms, the spirochaetes and fusiform bacilli of Vincent's angina being frequently, but by no means invariably, present; in other cases streptococci, and in still others *Bacillus coli*, have been found in the lesions of mucous membranes. The condition is a highly fatal one, for though spontaneous recovery may take place, the mortality of untreated cases is about 75 per cent. Very acute cases are met in which death occurs in two or three days. There are also chronic forms in which the illness lasts over several months, and in such cases relapses are apt to occur after the leucocytes have been restored to nearly normal and the patient has enjoyed good health, it may be for several months. Such relapses have been found to follow, in persons liable to this condition, upon a repetition of the drug which is regarded as an important agent in the cause of many of the cases.

In 1930, Turley and Shoemaker [3] found experimentally that the administration of phenobarbitone to dogs produced a marked reduction of their granulocytes, and in the past two years over 100 cases have been recorded by different observers in which a similar condition has been found in persons to whom amidopyrine had been administered in normal therapeutic doses over various periods of time. In a paper by Madison and Squier [3] in 1934, fourteen cases of agranulocytosis following the taking of amidopyrine are recorded, chiefly in the case of physicians, physicians' wives, and nurses. This remedy has been especially blamed when it has been combined with phenobarbitone. According to Herz,[4] various compounds of such remedies have been responsible for severe cases of agranulocytosis, including amidopyrine and certain compounds in which this drug is combined with barbiturates. Other possible causes have been stated to be benzol and arsphenamine, while quite recently [5] the administration of salts of gold

has been found to produce fatal purpura haemorrhagica with agranulocytosis. Another theory, based upon dietetic experiments on dogs, has been advanced by Miller and Rhoads,[6] who found that deprivation of vitamin B_2 produced a condition of stomatitis with anaemia, while the bone-marrow was found to show evidence of suppressed leucocytogenic function. This vitamin deficiency, however, cannot be more than a contributing factor to the development of agranulocytosis. The general body of evidence seems to indicate that some persons have a weaker leucocytogenic function of the bone-marrow than others, and that in such persons the administration of amidopyrine and other drugs of a similar character brings about a sensitization of the tissues which depresses the function of the bone-marrow and renders other tissues, especially mucous membranes, liable to bacterial invasion. It may be said that any case presenting the symptoms of fever combined with necrosing stomatitis or pharyngitis requires a careful examination of the blood, especially in regard to the condition of the leucocytes.

Treatment consists in the first place of avoidance of any of the drugs mentioned above in the case of persons who are liable to this condition. Considerable success has been obtained in cases which are not very acute by the administration of stimulants of leucocyte formation such as pentnucleotide, a mixture of the sodium salts of pentose nucleotides, administered by intramuscular injection. Nucleic acid may be used in the same way. Another form of treatment that has been recommended is the application of small stimulating doses of x-rays to the long bones. The septic throat is sprayed with some mild antiseptic and soothing solution.

A case of agranulocytosis under the writer's care presented the following features. The condition developed after nearly a year's suppuration about the mouth, and may have been due to wearing out of the leucoblastic tissues.

CASE.—A. E., a printer, aged 27, in 12/33 had an abscess at the root of the left lower wisdom tooth; the abscess extended from the mastoid region to the chin; it was opened and several septic teeth were extracted, he refused to have several other septic teeth removed and for the next nine months he had crops of pustules on the chin; in 10/34 an abscess developed on the right cheek, there was severe pyorrhoea of all the teeth, and he began to have difficulty in swallowing from inflammation in the throat. Admitted to hospital 29/10/34; temperature 102°, pulse 110, respiration 27; very thin and weak;

liver and spleen not enlarged; blood showed r.b.c. 1,600,000, Hgb. 16 per cent., w.b.c. 2600 of which 75 per cent. were lymphocytes and primitive cells; urine contained albumin and acetone. Transfused with 20 ounces of blood; general condition improved; on 2/11/34 blood showed r.b.c. 1,480,000, Hgb. 25 per cent., w.b.c. 4000 with less than 2 per cent. of polymorphs; sodium nucleinate given intramuscularly. On 3/11/34 patient weaker; w.b.c. 2600 with no polymorphs; swelling of abdomen and pleurisy on left side developed. On 4/11/34 blood showed r.b.c. 1,150,000, Hgb. 20 per cent., w.b.c. 1400 with no polymorphs, 3 per cent. of reticulocytes. On 5/11/34 died. Post-mortem examination showed ulceration and cellulitis of pharynx; acute peritonitis and pleurisy; no endocarditis; bone-marrow leucoblastic; culture from teeth and pharyngeal ulcer gave haemolytic streptococci.

Conclusions.—The condition of agranulocytosis developed in this case after nearly a year's suppuration about the mouth, and may have been due to wearing out of the leukoblastic tissues. There was no history of amidopyrine or similar remedy having been taken habitually.

II. Acute Leukaemia.

Acute leukaemia is probably a more frequent disease than statistics show, because of the difficulty in recognizing it unless a careful examination of the blood is made. It usually begins with a febrile attack accompanied frequently by enlargement of the tonsils and sore throat, so that it is almost invariably regarded at first as a passing attack of the nature of influenza. It is only when these symptoms fail to clear up after a week or more that some other cause is sought and a tentative diagnosis is then apt to be made of enteric fever or miliary tuberculosis, which, however, fails to receive support owing to the absence of the agglutination test characteristic of the former and the physical signs of the latter. The patient within a week or two from the onset usually shows some signs of purpuric eruption, and frequently of severe haemorrhages. It is not uncommon for such a haemorrhage following tonsillectomy, which has been carried out on account of the enlarged tonsils in this condition, to be the first sign that draws attention to the presence of a blood disease. In any case, a marked anaemia soon develops, accompanied by weakness, loss of weight, and increasing rise of temperature. The lymphatic glands soon enlarge, and the spleen is usually found to be palpable and sometimes to be greatly

enlarged with corresponding increase in size of the liver Nodules composed of masses of cells frequently develop under the skin or in the mucous membranes of the mouth or intestine, and these may ulcerate and produce severe haemorrhage If the blood be now examined, it is found to show a marked diminution of the red cells with still greater diminution of the haemoglobin and a low colour index, but the most striking feature is the presence of a great excess of white cells of a primitive type, usually lymphoblasts but in other cases premyelocytes and myeloblasts, or a mixture of these two types of white cells In rarer cases the excess of white cells is largely produced by monocytes The total count of white blood corpuscles in the earlier stages of the disease does not usually amount to more than 25,000 or 30,000 per c mm, but there is generally a rapid rise before the fatal termination An important point to notice, however, is that some cases presenting all the symptoms do not show for a time an increase of white blood corpuscles above the normal figures, but even in these cases the primitive nature of the cells can readily be recognized, such cases are sometimes called *aleukaemic leukaemia* The condition is almost invariably fatal within a few weeks from the commencement, and the disease runs a specially rapid course when it occurs in children Blood transfusion often produces temporary amelioration, and so also do applications of x-rays to the spleen and long bones

The following are two typical cases of acute lymphatic leukaemia under the writer's care

Case 1.—R C, aged 5, was quite well till after an attack of measles in 4/34 when his tonsils were enlarged, tonsils and adenoids removed 7/34, and recurring, were again removed 8/34, enlarged cervical glands noticed and bleeding from gums in 9/34 Admitted to hospital 5/9/34, temperature 98 4°, pulse 130, respiration 30, general enlargement of glands, liver and spleen much enlarged, blood showed r b c 1,930,000, Hgb 20 per cent, w b c 180,000 with 70 per cent of lymphocytes and lymphoblasts On 24/9/34 after four x ray exposures, spleen and glands much smaller and blood showed r b c 2,060,000, Hgb 22 per cent, w b c 4800, chiefly lymphocytes On 7/10/34 spleen was again rapidly enlarging and blood showed r b c 2,120,000, Hgb 40 per cent, w b c 270,000, of which almost all were primitive lymphocytes On 9/10/34 died, less than one month after he became seriously ill Post mortem examination showed marked enlargement of the spleen, liver, and kidneys, the bone-marrow showed great hyperplasia of the lymphoid

elements, lymphoblasts being very numerous, and there were numerous cells of a much more primitive type, there were a few myeloblasts but no myelocytes, no erythropoiesis, great infiltration of the other organs with lymphoblasts and lymphocytes

CASE 2.—K. D., aged 19, a well-known football player, was quite well till end of 9/34 when he had an attack of 'influenza' followed by loss of appetite, flatulence, enlarged cervical glands, and swelling of the abdomen, in 10/34 felt increasing weakness and had attacks of epistaxis. Admitted to hospital 20/11/34, showed marked pallor, temperature 99°, pulse 110, respiration 22, spleen enlarged to level of umbilicus, liver 3 inches below costal margin, some ascites, many enlarged glands, blood showed r.b.c. 3,000,000, Hgb. 45 per cent., w.b.c. 147,000 of which almost all were lymphocytes and lymphoblasts, numerous nucleated red cells. basal metabolic rate +86 per cent. 12/12/34 after five x-ray exposures and 10 c.cm. of campolon intramuscularly improved at first, and liver, spleen, and glands diminished at first but later enlarged rapidly, blood now showed r.b.c. 1,950,000, Hgb. 36 per cent., w.b.c. 300,000, chiefly primitive cells with a few myelocytes and polymorphs. 15/12/34 transfusion of 20 ounces of blood which was repeated three times more, and two more x-ray applications, after which blood showed r.b.c. 2,200,000, Hgb. 42 per cent., w.b.c. 74,000. 1/1/35 blood showed r.b.c. 1,470,000, Hgb. 32 per cent., w.b.c. 312,000, of which a few were small lymphocytes, most primitive cells, and a number myelocytes. 3/1/35 died thirteen weeks after illness began. Post-mortem examination showed enlargement of all lymphatic glands and nodes, and great enlargement of liver and spleen, bone marrow showed exceedingly active lymphoblastic reaction, but no leucoblastic and very little erythroblastic activity, infiltration of spleen, liver, kidneys, etc., with lymphoblasts and lymphocytes.

Conclusions.—In both cases the blood showed primitive lymphocytes in great numbers, temporary improvement followed deep x-ray applications to the spleen, the illness lasted in one case three and in the other thirteen weeks.

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RECENT WORK ON THE ANAEMIAS:

An Abstract Review.

GENERAL.

Classification and Diagnosis.—The importance of a correct classification of the anaemias as an aid to differential diagnosis is generally admitted, for accurate diagnosis is essential to adequate treatment. In this connexion the work of HADEN (Chicago) may be cited. He points out that an anaemia is a decrease in the haemoglobin below the limit of normal, which results from qualitative or quantitative changes in the erythrocytes. The normal growth of the red cells requires certain non-specific elements—protein, carbohydrate, mineral salts, vitamins—as well as two specific factors—iron and the antianaemic principle of the liver. Blood is constantly being destroyed and fresh erythrocytes are constantly being formed, passing through various developmental phases. The most active indicator of the activity of erythrocyte regeneration is the level of reticulocytes in the circulating blood. With a correct study of the blood and a careful history of the patient, a case of anaemia can almost always be correctly classified both clinically and haematologically. Haematological classification is based on the size and haemoglobin content of the red cell, as determined by laboratory examination, six groups being recognized :—

1. Normocytic and normochromic. volume index normal, colour index normal.
2. Normocytic and hypochromic: volume index normal, colour index low.
3. Macrocytic and hyperchromic: volume index increased, colour index increased.
4. Macrocytic and normochromic: volume index increased, colour index normal.
5. Macrocytic and hypochromic: volume index increased, colour index low.
6. Microcytic and hypochromic: volume index low, colour index low.

The factors in the production of anaemia are relatively few, but frequently more than one factor may be operative. Thus, with adequate specific treatment of pernicious anaemia an iron deficiency not infrequently develops if the response to therapy is rapid; again, infection is often a factor in the specific deficiency anaemias.

Discussing differential diagnosis, MATTHEWS (Liverpool) suggests that for this purpose and in order to avoid confusion the following classification will serve: (1) pernicious anaemia; (2) idiopathic hypochromic anaemia; (3) other deficiency anaemias (scurvy, etc.); (4) haemolytic anaemias; (5) secondary anaemias, due to malignant disease, infections, or haemorrhage; (6) aplastic anaemia; (7) splenic anaemia.

Whitby (London) deals with the value and interpretation of blood counts and states that when a patient merits a haematological examination it is as well that the first examination should be complete Re-examinations may be confined to relevant points Should it be impracticable to perform more than one simple examination, the haemoglobin estimation is of more value than the red cell count Leucocyte counts should always comprise proper total and differential counts, it is fallacious to attempt to estimate a total leucocyte count from the appearance of a blood film The importance of red cell size for determining a type of anaemia has led to the introduction of instruments, the most frequently used being Eve's halometer This cannot replace a proper haematological examination it should be used only as an adjuvant and then only by those practised in its use —it does not provide a short cut to the bedside diagnosis of pernicious anaemia

According to Schnabel (Philadelphia), the laboratory should be used only in part as an approach to the problems presented in diagnosis and treatment Exclusive reliance must not be placed on laboratory work in the study of anaemic patients and in control of their treatment, but its directional aid should be sought intelligently and the results evaluated in the light of clinical judgement and experience

Holiday, Kerridge, and Smith (London) hold that, notwithstanding the many investigations that have been made, it is impossible to estimate with accuracy the amount of haemoglobin in a given volume of blood, further, that the percentage of haemoglobin relative to a normal standard is accurate only for the apparatus employed and differs widely with different instruments They describe a method for the determination of the relative amounts of haemoglobin in different bloods, based upon a physical property of oxyhaemoglobin the measure of which is permanent For details of their method the original article should be consulted

Discussing the application of diagnostic criteria to treatment, Bethell (Ann Arbor, Mich) concludes that the study of the number, size, and haemoglobin content of the red blood cells gives an insight into the nature of deficiency anaemias and provides a rational basis for treatment Retarded rate of haemoglobin formation is most often due to a lack of iron, possibly associated with insufficient protein, pigment complex, and vitamins In pregnancy the anaemia caused by dilution of the blood persists because of absence of stimulus to increased blood formation together with a relative lack of iron This may be corrected, in large part, by long continued use of this metal, and it is suggested that medicinal iron should be given as a routine during the latter half of pregnancy Retarded maturation of the erythrocyte is commonly the result of a relative deficiency of the intrinsic or extrinsic factor of Castle

Aetiology —Reference was made some months ago (Prescriber, 1935 May, 174) to the discovery by Dodds and co-workers of the

presence in the posterior lobe of the pituitary body of a gastrotoxic factor—a substance capable of inducing a severe lesion of the acid-bearing area of the stomach. More recent work by DODDS, HILLS, NOBLE, and WILLIAMS (London) shows that this may have a bearing on the causation of certain anaemias. Injection of pituitary extract causes a temporary inhibition of the acid secretion of the stomach, which will not respond to histamine for several hours. After some days a severe anaemia develops, the blood count is greatly reduced and a reticulocytosis appears, indicating stimulation of the blood-destroying system, with marked anisocytosis and a definite macrocytosis. Further work is being done to investigate what appears to be a hormonal connexion between the posterior lobe of the pituitary, the stomach, and the blood picture.

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ANAEMIAS OF INFANCY.

The anaemias met with in infancy and childhood are numerous and varied, and differ in many respects from those of adults. In a lengthy article on the subject, PARSONS and SMALLWOOD (Birmingham) divide these into two main groups—the hypoplastic, anhaematopoietic or deficiency anaemias, and the haemolytic or erythronoclastic type. The first group includes *nutritional anaemia*, probably the most widely spread and important, *iron-deficiency anaemia* in older children, the anaemias of *coeliac disease* and *scurvy*, and several rarer forms. In the haemolytic anaemias the deficiency of circulating blood is the result of cell destruction, and the breaking down of the contained haemoglobin causes an increased formation of bilirubin which, circulating in the blood, gives a positive indirect van den Bergh reaction and may render the skin and conjunctivae icteric. Haemolytic anaemia of the new-born embraces three clinical entities —*icterus gravis neonatorum*, severe and often fatal, haemolytic anaemia *without* icterus gravis, and a variety *with congenital hydrops foetalis*. In later infancy and childhood haemolytic anaemias of all degrees of severity may be found, from the acute haemolysis of Lederer's anaemia to the more chronic von Jaksch's syndrome and the still more chronic acholuric family jaundice. This last, if severe, calls

for removal of the spleen, anaemias of the Lederer or von Jaksch type are best treated by intravenous transfusion of citrated blood

HELEN MACKAY (London) remarks that anaemia is diagnosed much too often in children of school age and not nearly often enough in babies, among whom it is extremely prevalent For diagnosis a haemoglobin estimation is necessary, as the child's appearance is not a trustworthy guide It is rare for a child to be born anaemic, but during the first month of life anaemia may arise through bleeding or haemolysis Anaemia developing between one and a half and four months is usually associated with a low birth weight—the so called early anaemia of premature babies Anaemia in a child between four months and four years is due probably to iron deficiency, it may be grafted on top of an anaemia due to infection Anaemia among school children is relatively uncommon except as a result of bleeding or as part of another disease The anaemia due to iron deficiency may be prevented by the supply of an adequate amount of iron To some extent this may be given through the pregnant mother, but to give iron to a nursing mother does not influence anaemia in the child as the iron is not increased in the milk Every baby from two months until over a year old should get 4½ grains of iron and ammonium citrate daily, beginning with a small dose and working up to the full dose within a week For treatment larger doses are needed 9 to 15 grains of iron and ammonium citrate or 4½ grains of ferrous sulphate daily

Anaemia associated with splenomegaly is much more frequent in infancy and early childhood than in adolescence and adult life According to ELLIS (London) the spleen enlarges readily in infancy in the course of many conditions including most generalized infections, which may also give rise to some degree of anaemia In addition a large group of cases exists in which enlargement of the spleen is directly related to the occurrence of anaemia Investigation of a child suffering from anaemia and splenomegaly will necessitate first the exclusion of a generalized infection In any severe anaemia transfusion may be required to save life, and will frequently hasten recovery in the milder cases Splenectomy is indicated in acholuric family jaundice, in Banti's disease and splenic anaemia when the platelets are reduced, and in severe anaemia secondary to purpura haemorrhagica In general, iron will benefit only those cases in which there is an iron deficiency, though recent work suggests that some benefit may be obtained from iron in true splenic anaemia

Nutritional Anaemia—While iron exists plentifully in many of the foodstuffs consumed by adults it is remarkably deficient in milk, which is the main diet for the first six months of life The normal infant has a store of iron in the liver, acquired from the maternal circulation during the latter part of pregnancy, but should this supply be inadequate, as in prematurely born infants or should it become exhausted through prolonged milk feeding, an iron deficiency will develop Anaemia due to nutritional deficiency is

hypochromic and microcytic in character, the haemoglobin being reduced out of all proportion to the fall in the erythrocyte count. Treatment consists in administration of iron and ammonium citrate, one grain per pound of body-weight being given daily in divided doses. To avoid gastro-intestinal disturbance very small doses should be given for the first few days until tolerance is established.

The age and sex incidence of nutritional iron-deficiency anaemia has been studied by DAVIDSON, FULLERTON, and CAMPBELL (Univ. of Aberdeen), who find that this form of anaemia is most pronounced at two age-periods—infants between the eleventh and twenty-third months of life and adult women who have had children. Observations on the haemoglobin levels of 3500 persons of both sexes and at all ages showed this anaemia to be present in 41 per cent. of infants under two years, 32 per cent. of pre-school children, 2 per cent. of school children, 16 per cent. of adolescent women, and 45 per cent. of adult women. It was absent in adolescent and adult males, except in association with organic disease.

FABER, MERMOD, GLEASON, and WATKINS (San Francisco) studied ten patients, aged between seven months and two years, with anaemia of the nutritional or iron-deficiency type, in whom gastric analysis after histamine showed noticeable secretory defect—free acid was absent in six and low in four. The blood was hypochromic and microcytic. Administration of soluble iron gave a striking response with reticulocytosis and increased size of red cells and rise in haemoglobin. A certain number of microcytes persisted. It appears that the average child in the latter half of its first year and for some time thereafter has a mild hypochromic anaemia. Children secrete little acid during the first two years of life and absorption of iron is therefore difficult; administration of soluble iron during this period is desirable. Iron-deficiency anaemia of childhood and hypochromic anaemia of adults bear a close resemblance to one another.

Discussing generally the anaemias due to nutritional deficiency, MINOT (Boston) remarks that these are due to a lack in the body of at least three classes of dietary substances—iron, vitamin C, and a mysterious substance contained in the liver. Iron-deficiency anaemias are hypochromic and usually microcytic and respond to iron treatment; those due to deficiency of vitamin C are normocytic or slightly microcytic and yield to administration of ascorbic acid; those due to deficiency of liver principle are macrocytic and usually are amenable to liver therapy. Prevention is of prime importance and calls for an optimum diet to allow the organism to develop without interruption.

Iron and Copper Therapy.—The prophylactic value of iron when supplemented with copper is well brought out in a series of observations by USHER, MACDERMOT, and LOZINSKI (Montreal). In a series of normal children (controls) the haemoglobin value fell sharply from the high level at birth after two or three months; it

rose slightly at five months and then fell slowly during the remainder of the first year A group of children receiving daily 1½ to 3 grains of iron as ferric glycerophosphate showed at the age of one year an average haemoglobin value of 15 per cent higher than the controls Another group receiving the same amount of iron plus 1 to 2 mg ($\frac{1}{60}$ to $\frac{1}{32}$ grain) of copper sulphate showed a haemoglobin value 19 per cent higher than the control group At 8 to 14 months the 'copper' group weighed more than the controls, and the 'iron' group weighed less In other respects, such as incidence and severity of infections, the children receiving iron and copper showed a definite advantage over the other groups Very similar results are reported by GOLDSTEIN from observations on 86 children, and he adds that iron combined with $\frac{1}{100}$ grain of dry thyroid gave results nearly as good as iron plus-copper

According to ELVEHJEM, the difficulties encountered in obtaining clinical data regarding the effect of copper in anaemia are very great The most reasonable conclusion seems to be that available iron accompanied by small but standard amounts of copper should be used in all cases showing reduced ability to form haemoglobin Copper is not concerned with the assimilation of iron, but with the transformation of the ingested iron into haemoglobin Experiments have shown that copper in moderate doses produces no ill effects, but it is well to keep in mind that after sufficient copper has been received to meet the requirements for normal metabolism, additional amounts are of no value and may do harm

Two years ago it was shown by GORTER, and it has since been confirmed by SACHS, LEVINE, and FABIAN, that in anaemic subjects the copper content of the blood is above normal and the same seems to be true of certain other diseases, such as leukaemia, malaria, nephritis, and tuberculosis High blood copper seems to be associated with low blood iron Whether this represents a compensatory response on the part of the organism, or is the result of its non-utilization in the formation of haemoglobin, is not known

Discussing the factors which affect the requirement, the absorption, and the utilization of iron, WITTS (London) remarks that the absorption of the iron contained in food or drugs is proportional to the ease with which the ferrous ions are liberated The soluble ferrous salts are the most active Iron acts as a nutrient and not as a stimulant for the blood-forming organs It repairs deficiencies which would not have occurred had the diet been satisfactory

Anaemia of Premature Infants.—Recent work by JOSEPHS (Baltimore) indicates that a deficient storage of iron and copper is not responsible for the early anaemia of premature infants Groups of infants of varying degrees of prematurity were observed as regards haemoglobin, erythrocytes, and reticulocytes, while at different stages of the experiment iron and copper were administered and the effects noticed Iron given from six to ten weeks after birth had no effect on the blood picture Then followed a short transition period

in which iron elicited a delayed response. After the third month iron therapy effected a prompt rise in reticulocytes and the usual subsequent increase in pigment and erythrocytes. In the few cases in which copper was given it appeared to have no demonstrable effect.

One of the dangers attending the life of the premature infant is infection, to which early anaemia predisposes the child. MACKAY (London) investigated a group of 150 infants, determining the haemoglobin during the first twenty-six weeks of life. It was found that injections of blood during that period left the haemoglobin level practically unaffected, the drop usually observed being greatest in the tenth to fourteenth week. The lowest level was about the same in the large as in the smaller infants, but investigation showed that iron had no effect in minimizing the haemoglobin drop in the smaller children. It is concluded that whenever progress and health have been satisfactory premature and immature babies do not show any severe anaemia during the first three months of life.

Congenital Anaemia of the New-Born.—It has already been remarked that a child is rarely born anaemic, but PASACHOFF and WILSON (New York) think that congenital anaemia of the new-born is more common than has been believed. They have found three cases in 6000 births, and they think that obstetricians should have their attention directed to its possibility. Congenital anaemia of the new-born may be defined as a hyperchromic anaemia of unknown origin that appears at birth or during the first two weeks of life in full-term and premature infants born of healthy parents. The anaemia usually makes its appearance between the third and the tenth day of life, but in some cases it has been noted at birth. Sometimes it occurs in several children of the same parents, but it has never been observed in the first-born. The tendency is towards spontaneous recovery, and for this reason many mild cases may go unrecognized. Iron, liver, and ultraviolet therapy have been employed with apparent success, but there seems to be no iron deficiency, and the tendency to spontaneous recovery makes it difficult to gauge the value of treatment.

Reporting a case of anaemia of the new-born, HENRY (Bentley, Canada) cites the following description of the condition: Anaemia of the new-born has been used to designate cases in which new-born infants, in the early days of infancy, develop pallor of a sheet-like whiteness as the only symptom. The blood picture is at first of a mild hypochromic type of anaemia, with the nucleated red blood cells moderately increased. He reports a case answering this description. The child when born was of a healthy colour, but developed jaundice after thirty-six hours. This faded from the fourth day and the child developed a pallor which increased to sheet-whiteness. Several transfusions were given and later liver extract was injected intramuscularly. On the twenty-eighth day the child was discharged in good condition, but liver extract was continued

irregularly for some time. Henry thinks that the child's life was saved by the transfusions, and that the liver extract supplied the curative factor.

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ANAEMIAS OF PREGNANCY.

DAVIES (London) divides the anaemias occurring during pregnancy into two groups—the hypochromic, which is relatively common, and the macrocytic, which is rare in this country but fairly frequent in the tropics, especially in India A mild form of the hypochromic type is common among women in the industrial areas and is due probably to poor feeding The healthy woman usually passes through pregnancy without any serious fall in her blood count. Anaemia may show itself during the first pregnancy, but it is more common in multiparae Usually the symptoms are more pronounced during the last three months when the foetus is storing up iron from the maternal circulation In the hypochromic type the haemoglobin is frequently around 40-50 per cent while the red cells are four millions, the colour index is therefore low It will usually be found that the patient's diet is deficient in iron-containing foods. this should be seen to and iron therapy instituted It is

probable that much disability and ill-health associated with pregnancy could be avoided by the early recognition of this disorder. The macrocytic type resembles pernicious anaemia in character, except that it frequently clears up spontaneously, which pernicious anaemia never does. Treatment is the same as for pernicious anaemia, and should be instituted early.

MACKAY (London) ascertained the haemoglobin level in 368 women of the hospital class—pregnant or mothers—and found it to average 85.5 per cent., which is 13.7 below the average for healthy women (98.26). Less than one-third of the total had a haemoglobin level of 90 per cent. or over. The degree of anaemia among the women was of a similar order to that existing among babies of six to twelve months old of the same social class. This anaemia of babies is sufficient to double their morbidity-rate. By analogy it is probable that anaemia is an important factor in lowering resistance to infection among women. Mackay urges routine iron therapy of expectant mothers and of babies.

IRVING (Syracuse, N.Y.) reports a study of the hypochromic anaemia of pregnancy occurring in his locality. He concludes that it is caused by a constant drain on the copper and iron reserve of the mother by the demands of the growing foetus. It should be called 'nutritional anaemia of pregnancy,' as it is analogous to the nutritional anaemia of infancy. Administration of copper and iron effects a gradual improvement in both red cell count and haemoglobin levels; diet alone does not seem to furnish a sufficient amount of the basic metallic elements.

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PERNICIOUS ANAEMIA.

Aetiology.—*The researches of Castle and associates, of Boston,* referred to in previous reviews, point to pernicious anaemia being a deficiency disease conditioned by the lack of a specific intrinsic factor present in normal gastric juice. This factor is different from any digestive ferment, and its function is to interact with an extrinsic factor in the food to produce specific haematopoietic effects. Pernicious anaemia may occur in three ways—lack of intrinsic factor in the stomach, lack of extrinsic factor in the diet, or failure to absorb or utilize the product of their interaction. So far all cases of pernicious anaemia studied in relapse have been due mainly to lack of the intrinsic factor. Certain other macrocytic anaemias, such as that occurring in the tropics and the anaemia accompanying sprue, have been treated successfully with suitable diets, which points to a lack of extrinsic factor.

MEULENGRACHT (Copenhagen) has made a study of the glands of the stomach in relation to pernicious anaemia, and he finds that the pyloric glands alone are responsible for the secretion of Castle's intrinsic factor The pyloric glands are distinct from the peptic glands the latter produce hydrochloric acid while the former secrete the antianaemic factor Pernicious anaemia, he says, is caused by atrophy or inactivity of the pyloric glands He suggests that preparations of desiccated stomach intended for treatment should be made from the pyloric glands alone

Treatment.—The effect of modern therapy on the length of life is well brought out by STOCKS (Medical Statistical Officer, London), who presents figures showing that since the introduction of the new methods of treatment in recent years there has been an average lengthening of life of all persons afflicted by pernicious anaemia in England and Wales amounting to three and a half years He shows certain changes in the distribution of deaths by ages, which are explained by a greater lengthening of the duration of life for the young than for the old patients, three and a half years being the average for all ages

MILLS and HERRING review the histories of fifty six cases treated at the Royal Berkshire Hospital and show that the condition of all patients receiving uncontrolled treatment was unsatisfactory and that in every case the blood picture of such patients was improved by more efficient treatment They suggest that the only practicable method of dealing with the maintenance treatment of these cases is the formation of haematological clinics where dosage can be controlled by regular blood counts and haemoglobin estimations

Summing up the general principles of treatment, WILKINSON (Manchester) states that the fundamental principle to be recognized is that pernicious anaemia is a permanent deficiency disease requiring adequate replacement therapy for life Therapeutically active preparations must be employed and the progress of the patient controlled by regular blood counts and suitable adjustment of the dose Treatment must be so administered that satisfactory improvement takes place in all the systems involved, and not controlled solely by the blood picture Thus the fact that a normal blood count is regained must on no account be taken as a sign to reduce or discontinue treatment if, for example, glossitis or diarrhoea or spinal cord involvement is still evident, for these are just as important signs of insufficient treatment as is a low blood count

Dealing with the influence of diet and other factors on haemoglobin regeneration, WHIPPLE (Rochester, N Y) shows how liver stands first as a diet factor while iron is the most important inorganic element One curious point is brought out by his experiments human liver (obtained at autopsy from healthy subjects) is 60 per cent more effective in causing haemoglobin regeneration than liver obtained from animals, even diseased human liver gives better results than healthy animal liver

Liver and Stomach Therapy.—In the Nobel Lecture at Stockholm MINOT (Harvard Univ.) outlined the development of liver therapy in pernicious anaemia. He showed how he and Murphy were led to their original experiments, and how the administration of raw liver came to be replaced by liver extract, at first by mouth and later parenterally. By the parenteral route liver extract is at least 30 to 50 per cent. more potent than by the mouth and can be given in much smaller doses. For parenteral administration a specially prepared extract is required, ordinary liver extract (B.P.) being unsuitable. It is essential that sufficient liver extract be given to supply indefinitely all demands of the body for the antianaemic principle and to provide an adequate reserve supply. The grave error in treatment is to prescribe too little liver extract; when there is any doubt more rather than less should be given.

GARDNER and WOOD (Melbourne) discuss the problems arising in the treatment of severe pernicious anaemia and describe three cases having erythrocyte counts of a million or less which were treated with massive intramuscular doses (24 ml.) of liver extract ('campolon'). The patients were in severe relapse and all recovered, the response in one case being described as dramatic. The object of treatment should be, first, to bring the red cell count and haemoglobin percentage back to normal as rapidly as possible and, secondly, to maintain this state of normality by means of a maintenance dose. When the haemoglobin and erythrocyte levels begin to fall injections must be resumed. Emphasis is laid on the importance of the reticulocyte response in judging the effect of treatment. In their experience the average time required for a maximum reticulocyte response is: (*a*) massive intramuscular dose, two to five days; (*b*) intramuscular small divided doses (2 to 4 ml. daily), four to eight days; (*c*) oral administration of fresh liver or liver extracts, six to ten days.

SCOWEN and SPENCE (London) report six cases treated with a concentrated protein-free liver extract administered intramuscularly. The preparation used was 'pernaemon forte' and it was found that after a single injection (8 ml. usually being adequate) the blood returned to normal within four or five weeks. With a maintenance dose of 5 ml. every four to eight weeks the blood count could be kept at a normal level.

Discussing those cases which are resistant to liver therapy, PINEY (London) indicates some of the commoner causes of failure and suggests means by which they may be overcome. He emphasizes the superiority of intramuscular injection and the possibility of keeping the blood in good condition with an occasional small dose. Of the causes of resistance to treatment the first is the presence of a septic focus, and the commonest infection in pernicious anaemia is pyelitis. The urine should be examined even if there are no symptoms suggestive of pyelitis. Another cause is mild hypothyroidism: in such cases small doses of thyroid will often remove the resistance. A third cause is arteriosclerosis, the condition of the arteries, not the

raised blood-pressure, being the cause of resistance In such cases larger doses of liver extract may be necessary Lastly, it is not uncommon to meet with patients whose red corpuscles are below normal and whose blood will not improve beyond that point however much liver extract may be given In these cases iron is helpful and it is usually safe to stop the iron when the blood has become normal In all cases removal of the inhibiting condition will reduce the number and size of the injections necessary

Mention has already been made of the importance of ascertaining the reticulocyte response in judging of the effectiveness of treatment The interpretation of reticulocyte reactions is the subject of a lengthy article by MINOT and CASTLE (Harvard Univ) who show that a careful quantitative estimation of the percentage of reticulocytes appearing in the peripheral blood gives an accurate measure of erythropoietic activity In anaemia with an aplastic marrow few, if any, reticulocytes are found, in anaemia with an active marrow they are many, in pernicious anaemia, where marrow activity is arrested, the number of reticulocytes varies The reticulocyte count is of special value as an index of the effectiveness of treatment their output is strictly related to the initial number of red cells and haemoglobin, and therefore furnishes an extremely accurate indication of the efficacy of treatment

Attempts to isolate the haematopoietic principle present in liver have hitherto been unsatisfactory in their results Recently, however, DAKIN and WEST (New York) have succeeded in separating a substance which has proved clinically effective in causing remission in pernicious anaemia The substance has not been crystallized and appears to be a mixture, but it seems to contain the whole of the haematopoietic principle and to be worthy of consideration The process of separation is based on the removal of inactive material by means of alcoholic calcium acetate, followed by separation of the active material by various precipitants About 30 mg (½ grain) of this substance caused a perceptible reticulocyte response in pernicious anaemia patients, while 80 mg (1⅓ grain) gave a maximal response The substance is inactivated by alkalis, and while its chemical nature has not yet been definitely ascertained it is probably a derivative of a polypeptide

Modified Liver Extracts —Three years ago (see PRESCRIBER, 1934, Feb , 60 61) it was shown by Herron and McEllroy (Philadelphia) that autolysis so increased the potency of liver extract as to reduce the oral dose to that used for intramuscular injection Fresh beef liver was treated with weak hydrochloric acid, incubated and filtered, the filtrate being the product employed Recent work by CASTLE and STRAUSS (Boston), however, goes to show that the claim of increased activity for this product has not been substantiated The haematopoietic action of liver, they say, does not depend on post-mortem autolysis, and autolysates of liver made by Herron and McEllroy's process have less haematopoietic activity than the

amounts of liver from which they are derived, as measured by the reticulocyte response.

Mention was made in this place a year ago (PRESCRIBER, 1935, Feb., 63) that addition to liver extract of a small amount of fresh stomach tissue is said to produce a very active preparation which can be given orally and is some three times as active as liver extract and five times as active as stomach tissue. This preparation, called *Extralin*, is made by incubating the Cohn fraction D from liver with minced fresh hog's stomach, adjusting to $pH=5$, and drying *in vacuo*. The product is put up in capsules of 0·5 gm., each representing about 20 gm. of fresh liver and about half that quantity of fresh stomach. The average dose is four capsules (2 gm.) thrice daily; the maintenance dose is somewhat less, but varies with the individual case. This product is still more or less in the experimental stage; reports indicate that it compares favourably with liver extract orally administered. It has been found to give specially good results when combined with iron, and a preparation *Lextron* has been issued containing liver-stomach concentrate, iron and ammonium citrate (green), and vitamin B complex.

The work of FOUTS, HELMER, and ZERFAS (Indianapolis) on gastric juice and its haematopoietic factor was mentioned last year (PRESCRIBER, 1935, Feb., 63). These workers now show that the potency of liver extract may be increased by incubation with normal human gastric juice. Liver extract was incubated at 40° C. for two to four hours with varying amounts of human gastric juice. The preparation was given by mouth for ten days to patients having pernicious anaemia in relapse. A maximal reticulocyte response followed the administration of 4 gm. of liver extract which had been incubated with 100 ml. of gastric juice; smaller amounts than 4 gm. were not effective, and at least 50 ml. of gastric juice was necessary to produce maximal reticulocytosis when daily doses of 4·5 gm. of liver extract were given.

Desiccated Stomach.—Reference has been made earlier in this review to the work of MEULENGRACHT (Copenhagen), who finds that the pyloric glands alone furnish the intrinsic factor of Castle. He suggests that preparations of desiccated stomach intended for treatment of pernicious anaemia should be made from the pyloric glands alone.

Congo Red.—MASSA and ZOLEZZI (Parma) noticed accidentally that the blood condition of a patient with pernicious anaemia improved after the injection of congo red, and they accordingly tried the treatment in eleven cases. They employed a 0·5 per cent. solution of the dye in a 0·5 per cent. solution of sodium chloride; this was given intravenously daily or every second day for five or six injections, and after an interval of several days a new series of injections was given, the total number being between fifteen and thirty-eight. The result was that the blood condition in all cases returned to nearly normal. In three other cases the combined use

of liver and congo red acted favourably, though the amount of liver was not sufficient to produce that effect In three more cases congo red had no effect, and liver had to be given

These results have since been confirmed by MERMOD and DOCK (San Francisco) In two cases of mild pernicious anaemia injections of 1 5 per cent congo red in 6 per cent dextrose caused a rise in reticulocytes comparable to that effected by intramuscular liver extract Experiments on guinea pigs confirmed its action Mermod and Dock suggest that congo red acts by neutralizing toxic substances that may be haemolytic

Subacute Combined Degeneration —Nervous symptoms due to combined degeneration in the spinal cord are often present in cases of pernicious anaemia and may be an early feature preceding any complaints due to the anaemia COMRIE (Edinburgh) cites a case in which intense tingling of the hands was the only complaint and yet the blood when examined showed only 2,400 000 corpuscles with a colour index over 1 3 and a film characteristic of pernicious anaemia while a test meal showed achlorhydria

Some observers have reported cases in which mental changes were associated with pernicious anaemia OSGOOD (Wauwatosa Wis) expresses doubt that such effects are directly due to the anaemia He has examined a number of cases in which these conditions were associated and he finds little, if any, evidence to support the assumption that pernicious anaemia can cause psychoses or that mental changes may be a manifestation of pernicious anaemia in the same sense as neurological changes may be Those patients who develop mental changes usually show a predisposition to mental illness as indicated by the family or past history Osgood concludes that the association of psychoses with pernicious anaemia is probably largely incidental

The value of liver therapy (intramuscular liver extract) in the treatment of subacute combined degeneration was mentioned in our review last year (PRESCRIBER 1935 Feb 62) and since then other favourable reports have appeared Among these may be mentioned one by STRAUSS SOLOMON, SCHNEIDER, and PATER (Boston) who state that twenty six patients with pernicious anaemia and advanced subacute combined degeneration of the spinal cord were treated by the intramuscular injection of liver extract for an average period of thirty four months The dose in each case was based upon individual requirements Complete arrest of the neural lesions occurred in every case Eighty other patients with pernicious anaemia and little or no neurological disturbances were treated in the same manner over an average period of three years In none of these patients was there any evidence that spinal cord lesions progressed or developed under treatment It is concluded that by appropriate parenteral liver extract therapy the spinal cord lesions of pernicious anaemia may be prevented from developing or, having appeared may be completely arrested

FARQUHARSON (Toronto) emphasizes the importance of rest as well as liver therapy in such cases. Definite improvement occurs under treatment with prolonged rest and adequate liver therapy in those whose neurological symptoms are of relatively short duration. The best results are obtained when potent liver extracts are administered intramuscularly. It is impossible in any given case to predict what the necessary dose will be, and it is suggested that the initial dosage should be twice or three times that commonly used in the early treatment of patients suffering from pernicious anaemia without involvement of the spinal cord.

Conditions Resembling Pernicious Anaemia.—The main features of pernicious anaemia are recognized as (*a*) a megalocytic anaemia, (*b*) gastric achylia, (*c*) frequent involvement of the central nervous system, and (*d*) a characteristic response to specific treatment. Certain other megalocytic anaemias have been found to resemble pernicious anaemia in one or more of these features but not in all. This matter is discussed by WILKINSON and ISRAELS (Manchester) in an exhaustive paper in which they describe a group of megalocytic anaemias that cannot satisfactorily be fitted into any known classification, although in many respects they closely resemble pernicious anaemia. Hitherto the members of this group have been regarded as anomalous examples of pernicious anaemia either because they fail to respond to liver therapy or because they show free hydrochloric acid in the gastric juice. Examination of a number of such cases shows the condition to be a distinct clinical entity. It is rare, showing about one per cent. of the frequency of pernicious anaemia, with which it is usually confused. These workers believe that this anaemia may be due to an inability to utilize, or possibly to mobilize, the antianaemic principle necessary for the correct maturation of the megaloblasts, even though this principle may be present in the body. On this hypothesis they propose the term 'achresthic' anaemia, from χρῆσθαι, to utilize. The condition is easily recognized and differs essentially from pernicious anaemia and the so-called haemolytic anaemias, with which it is most likely to be confused. Seven cases are described: all showed free hydrochloric acid in the stomach and all were resistant to liver treatment. The definition offered is: 'A rare but severe hyperchromic megalocytic anaemia due to lack of utilization, or mobilization from the storage depots of the body, of the anti- (pernicious) anaemia principle found in liver. It is characterized also by a normal or almost normal gastric acidity, no disturbance of the gastro-intestinal tract or central nervous system, no pyrexia or evidence of haemolysis, and a lack of, or poor response to, antianaemic treatment.' The sexes are about equally affected and the age of onset is much more variable than in pernicious anaemia.

MCGOWAN (Aberdeen) thinks that the separation of these cases as a distinct group is hardly justified, inasmuch as these cases appear to be simply examples of a more malignant and intractable involve-

ment of the bone marrow, while the absence of achlorhydria, etc, demonstrates that this has no primary relationship to the production of the disease McGowan divides the anaemias characterized by large red blood cells into two groups—megalocytic and macrocytic The appearance of the megalocytic group depends essentially on organic changes in the bone marrow and is associated with a return to the early embryo form of erythropoiesis, in the macrocytic group the bone marrow is healthy and the phenomena in the blood are caused by a deficiency of the antianaemic factor, whether due to absence of extrinsic or intrinsic factor, to non-absorption of the product of their interaction, or to failure of the liver to elaborate this to the fully formed liver agent [Whether or not it is justifiable to include as a distinct entity the cases described of Wilkinson and Israels, one can but deprecate the indiscriminate coining of new terms, especially when such terms rest merely on a hypothesis The word 'achresthic' is cumbrous and suffers from a super abundance of consonants if such a term is to be adopted, 'achresic' (χρησις, utilization) would be more euphonious —EDITOR]

KERSLEY (Bath) describes five cases of atypical megalocytic anaemia In one the stomach showed normal acidity and the condition reacted well to liver therapy In the second the megalocytic anaemia developed from a microcytic anaemia in a woman with normal gastric acidity and the condition failed to react to liver or to iron therapy until after blood transfusion Two cases resembled pernicious anaemia except that free hydrochloric acid was present in the stomach The fifth case at first reacted to iron and later became definitely megalocytic, showing no response to iron or liver therapy and reacting only to blood transfusion The anaemia was accompanied by menorrhagia and at times by mania The patient died and the post mortem findings were those of intense normoblastic activity in conjunction with fatty degeneration of the vital organs

'Haemolytic anaemia appears in many guises, between acholuric jaundice and the acute type described by Lederer we may recognize an ascending series of anaemias of increasing clinical severity These cannot readily be classed as separate entities since their essential features are the same' This is the opening sentence of an article by LOVIBOND (London) in which he reports a case of subacute macrocytic haemolytic anaemia in a girl aged 22 years Treatment by liver, iron, blood transfusion and splenectomy all failed to improve the patient's condition and she died with the complication of a streptococcal infection The fragility of the red cells was normal, autopsy showed acute necrosis of the liver The probable cause of the anaemia was thought to be either acholuric jaundice or an infective process

BOX and GILL (London) describe a case presenting symptoms, signs, and blood picture closely resembling pernicious anaemia with in addition syphilis The disease failed to respond to adequate doses of stomach extract, but showed a gratifying improvement under

antisyphilitic measures alone This does not appear to have been a natural remission · the improvement both in general condition and in blood picture was so steadily progressive, particularly after neoarsphenamine treatment was instituted, that there seems little doubt that the one was intimately connected with the other It is suggested that either a syphilitic lesion in the liver prevented the storage of antianaemic principle, or the bone-marrow was in some way affected by the spirochaete

PELLEGRINI (Pavia) describes a case of pseudo-pernicious anaemia occurring in a case of chronic lead poisoning It was difficult to decide whether the lead intoxication had induced a particular type of anaemia of a rather pernicious form, or whether an anaemia from lead poisoning had been superadded to a pernicious anaemia In course of time some of the signs of lead anaemia disappeared, but those of pernicious anaemia persisted

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OTHER TYPES OF ANAEMIA

Aplastic Anaemia —This is defined as a rare condition in which the bone marrow cells cease to produce leucocytes in sufficient amount to compensate for their destruction (Dorland) As granulocytopenia may form part of the blood picture in addition to diminution of the red cells and platelets HOLMES (London) made an attempt to treat two cases with pentose nucleotide while maintaining the red cell count at a reasonable level by blood transfusion The attempt failed and both patients died without any real improvement having taken place

IMRIE (Glasgow) reports a case in which aplastic anaemia followed administration of neoarsphenamine It appears that the organic arsenical drugs used in the treatment of syphilis can act as powerful poisons to the bone marrow and that their toxic action may not become manifest until some weeks after cessation of treatment In this case blood transfusion iron therapy liquor arsenicalis liver extract and thyroid were given in the course of treatment and the patient recovered It is interesting to note that the appearance of reticulocytes in considerable numbers coincided with the administration of thyroid

BALDRIDGE (Iowa) records three cases of anaemia in women who had dyed their hair just before the application of permanent waving' It is suggested that the heat and ammonia used in the permanent wave process might either change the dye chemically or by induction of hyperaemia of the scalp lead to its absorption in unusual amounts The three cases all showed a macrocytic anaemia resembling that of pernicious anaemia but in addition to failure to respond to liver therapy the history course and confirmatory tests for pernicious anaemia were negative, and features characteristic of aplastic anaemia were observed

Hypochromic or Microcytic Anaemia —This form of anaemia has attracted considerable attention during the past few years Many names have been given to it one of these being achlorhydric anaemia though it has been shown that achlorhydria is not a constant feature It is much more common than pernicious anaemia to which it bears no relation and from which it differs in several important respects The blood shows a microcytosis and hypochromia of the red cells without marked diminution in the number of erythrocytes hence the volume and colour indexes are low

Glossitis is present and sometimes leads to a troublesome dysphagia (Plummer-Vinson syndrome) The disease is most common in women between 40 and 50 years of age, and appears to be due to iron deficiency, the result of digestive defect consequent upon the strain of child-bearing Iron is a specific remedy it is usually given in the form of iron and ammonium citrate in large doses—30 to 40 grains thrice daily after meals, iron pill (Blaud's pill) may be given but appears to be less reliable Liver diet has no effect

HARTFALL (London) reports a study of forty cases of anaemia following gastric operations The hypochromic type is much more common than the hyperchromic form simulating pernicious anaemia The amount of stomach removed has no constant relation to the development of anaemia, and the condition is more common in women than in men and most frequent between the ages of 40 and 50 years The presence or absence of free hydrochloric acid does not affect its development The clinical features are those encountered in hypochromic anaemia as described in the previous paragraph Post operative treatment should include an adequate diet

APPERLY (Richmond, U S A) shows that a direct relationship exists between the red cell content of the blood and gastric acidity When the former falls to about half or two-thirds normal, free acid disappears from the stomach

WOTZKA (Breslau) differentiates various types of gastrogenic anaemia, all associated with achlorhydria or achylia One, characterized by trophic changes in the finger-nails and corners of the mouth and a hypochromic microcytic blood picture, responds to the administration of iron and hydrochloric acid but not to liver, being distinct from pernicious anaemia in which the blood picture is hyperchromic and macrocytic The third type tends, after a more or less prolonged interval, to follow resection of portions of the stomach, it is also hyperchromic and does not respond to liver or to any drug treatment

Hookworm Anaemia —A form of anaemia that has recently attracted notice is a hypochromic microcytic anaemia occurring in persons infested with hookworm—*Ankylostoma duodenale* or *Necator americanus* Some controversy has arisen regarding the cause of this form of anaemia some hold that it is the result of depression of the bone marrow due to toxins liberated by the parasites, while others regard it as a nutritional deficiency assisted by some action of the parasites inhibiting the assimilation of iron BANERJEA (Calcutta) reports the case of a boy, aged 12 years, who was treated exclusively with massive doses of iron for a period of four months The haemoglobin value rose from 10 to 93 per cent and the red blood cell count from 1,020,000 to 5,840,000 per c.mm, in spite of heavy persistence of ova in the faeces Banerjea concludes that an interference with the assimilation of iron probably plays a greater part in the production of hookworm anaemia than intoxication of the bone marrow or loss of blood

Lederer's Acute Haemolytic Anaemia —JOULES and MASTERMAN (Birmingham) report four cases of this condition, which they regard as one of the most important of the smaller classes of recently recognized anaemias, in view of its amenability to treatment and its possible confusion with pernicious anaemia The condition is probably more frequent than has generally been recognized Reticulocytosis, usually not exceeding 15 per cent, has been present in all cases where an estimation has been made The red blood cells have shown anisocytosis, poikilocytosis, and basophilic punctation The colour index is usually at or above 1 All cases have pyrexia Blood transfusion is the only treatment, and is usually successful

Rheumatism and Anaemia —The frequent association of anaemia with chronic rheumatism is well known The condition has been studied by COLLINS (Harrogate), who remarks that anaemia is an important complication of rheumatism as it causes the patients to suffer more from their disabilities The anaemia is due to diminished haemoglobin in the blood with a relatively insignificant fall in the red cell count It is common among patients with chronic rheumatic conditions and is most common among females The severer degrees are found only in cases of atrophic arthritis Deficient gastric secretion is not a constant factor The anaemia accompanying rheumatism is not a specific disease it is a simple hypochromic anaemia secondary to the disease process

Scurvy, Anaemia of —That anaemia occurs in scurvy is recognized, but until recently it was believed to be due simply to the undernutrition and the haemorrhages characteristic of the condition It has recently been shown however, that in experimental scurvy the anaemia is largely dependent on the retardation of the maturation of the erythrocytes in the bone marrow, the result of deficiency in vitamin C, and that orange juice produces a reticulocyte response DUNLOP and SCARBOROUGH (Edinburgh) have studied two cases of human scurvy with particular reference to the haematopoietic effect of ascorbic acid In one case the diet of the patient, an unemployed man, was far from nourishing, being deficient in both iron and vitamin C This diet was continued while he attended as an out patient and ascorbic acid, 60 mg (1 grain) daily, was given The symptoms of scurvy abated, the anaemia disappeared, and the patient appeared to remain in good health afterwards while still on the same diet A definite degree of reticulocytosis was observed during treatment, with a rapid increase in the red cell count and a rise in haemoglobin It is evident that ascorbic acid is capable of being stored in the body and of exerting its effects for some time The second case was milder and the anaemia was less marked, but the conditions were otherwise similar and ascorbic acid had the same effect on the blood Dunlop and Scarborough suggest that if vitamin C has a specific effect on the anaemia of scurvy, distinct from its effect in controlling the haemorrhages,

then it is possible that a deficiency of this substance may be an additional factor in producing anaemia in working-class populations even in the absence of other signs and symptoms of frank scurvy

WOOD (Melbourne), dealing generally with anaemia in childhood, refers to anaemia of scurvy Children with scurvy, he says, are anaemic for several reasons Their diet may be lacking in iron and vitamin B as well as in vitamin C, the repeated small haemorrhages cause a drain on the iron stores, the appetite is poor, and finally vitamin C may be an essential factor in the production of red blood cells Orange juice will cure the anaemia, but iron may have to be given also

Sickle-Cell Anaemia.—This is a hereditary blood dyscrasia, with a symptomatology that frequently leads to its confusion with other diseases In the active phase the erythrocytes become elongated and sickle-shaped; in the latent phase sickling is absent at first but can be seen after the fresh blood specimen is some hours old Anaemia is pronounced and muscular pain is constant Ulcers of the legs are common Clinically, the disease closely resembles familial haemolytic jaundice, but without the increased fragility of the erythrocytes or the enlarged spleen usually present So far as has been known, the disease is confined to negroes, and nearly all the literature relative to it comes from America Quite recently several reports have appeared which tend to show that the disease is not restricted to negroes, although in America it is often difficult to be quite certain of the absence of negro blood COOKE and MACK report the existence of the disease in a family which for four generations at least was known to have no admixture of blood The father had sickling of the blood without anaemia The youngest child had an enlarged spleen and anaemia Transfusion effected only temporary improvement and splenectomy had the same temporary result A three-year old sister gave the blood picture of sickle-cell anaemia, but without sickling, which, however, showed later in the blood of both children

Splenic Anaemia.—Notwithstanding research the cause of splenic anaemia is still unknown The condition is marked by splenic enlargement and anaemia and occasionally progresses with the development of cirrhosis of the liver with jaundice and ascites, in which case it is known as 'Banti's disease' Whether or not it is a primary disease of the spleen, it is known that removal of that organ may effect remarkable improvement in the patient's condition More recently it has been found that simple ligation of the splenic artery will, by causing atrophy of the spleen, bring about clinical results similar to those of splenectomy, even when cirrhosis of the liver has developed. WATSON (Invercargill, New Zealand) reports a case in which this procedure was effective The patient, a woman aged 26, had a history of nineteen years of splenomegaly Ascites had been present for six months and the case seemed hopeless,

yet ligation of the splenic artery was followed by rapid reduction in the size of the spleen and improvement in general health which had lasted for three years after operation Ligation of the splenic artery appears to be a safe procedure provided it is done sufficiently far from the spleen to avoid interference with the communication between the splenic and left gastro epiploic arteries

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AGRANULOCYTOSIS

This blood condition which has only comparatively recently (1922) been recognized as a clinical entity is characterized by extreme reduction in the number of circulating granular leucocytes The symptoms are fever ulcerative stomatitis and sometimes jaundice and the disease is usually rapidly fatal It occurs most frequently in middle aged women Quite recently a connexion has been traced between its incidence and the use of certain drugs such as amidopyrine and other synthetic compounds containing the benzene ring These drugs by no means invariably produce the disease the sequence is only occasional and in the great majority of cases no such effect results The subject is dealt with at length by Dr J D Comrie in the present issue and for further information the monograph by ADAMS recently published by the Ministry of Health may be consulted

Aetiology —WILLCOX (London) discussing the aetiology of the condition says that there appears to be a defect of the bone marrow, the myeloid tissue being unable either to produce polymorphonuclear cells or having produced them to deliver them into the blood stream The condition is closely allied to leucopenia and is indeed a variety of it the granular leucocytes being specifically vulnerable

He has never seen a case of agranulocytosis from amidopyrine although he has often prescribed the drug, and he believes that certain persons are peculiarly susceptible to its action.

The relationship of drug therapy to agranulocytosis is exhaustively discussed by KRACKE and PARKER (Emory Univ., Georgia). They review the literature very thoroughly, having collected as many as 172 cases in which the disease has followed the administration of certain drugs, and they conclude that it is now well established that amidopyrine, dinitrophenol, and possibly other closely related drugs, are to be incriminated as aetiological agents. They admit that amidopyrine is a valuable drug and that it has its place in therapeutics, but they hold that it should be used under closely controlled conditions. It ought not to be freely obtainable by the public, and physicians should prescribe it with care and mark their prescriptions 'not to be repeated.'

Laboratory experiments are reported by BOLTON (Kansas City) in which the effects on the blood count of amidopyrine, barbitone, phenylhydrazine, and benzene were studied in a series of dogs. One animal showed a moderate leucopenia after amidopyrine, one after benzene, and anaemia with leucocytosis was observed in one which had received phenylhydrazine, but the pathological findings were not conclusive. STENN (Chicago) reports that administration of amidopyrine to guinea-pigs, rabbits, and monkeys failed to produce any appreciable granulocytopenia. It is suggested by Bolton that in some persons transformation products possessing toxic properties are formed, and that by virtue of individual supersensitiveness these toxic properties result in arrested maturation of the myeloid elements.

As already indicated, a large number of cases have been reported in which agranulocytosis followed administration of amidopyrine or similar drugs; many of these were recorded in our review last year (PRESCRIBER, 1935, Feb., 67). Of those more recently published the following may be mentioned. HANSEN and HOLTEN (Denmark) report the case of a woman aged 25, who in the course of fourteen months had taken 380 gm. (over 12 ounces) of amidopyrine before symptoms of sensitivity appeared. Examination of other cases in the hospital (all attributable to this drug) showed a high incidence of endocrine disturbances. Attempts were made to discover whether patients with endocrine disorder show greater leucocyte response to amidopyrine, but no such tendency could be demonstrated. HEWLETT (London) reports a case in which the patient had been taking amidopyrine off and on for several years whenever he felt 'a cold coming on': he was 60 years of age and he died in hospital. FOSTER and DOUGLAS (Stanmore) record a case of extreme granulopenia, though not of true agranulocytic angina, in which the patient had been taking certain synthetic drugs for rheumatoid arthritis. The case responded to treatment with pentnucleotide. A case, due to amidopyrine and responding to pentnucleotide, is reported by SMITH (Manchester), and another, due evidently to a barbiturate, is

described by RANSON (Shanghai) A fatal case of agranulocytosis with purpura haemorrhagica following gold therapy is recorded by ELLMAN and LAWRENCE (London) In this case injections of an organic gold salt had been given as treatment for rheumatoid arthritis

HARRIS and SCHATTENBERG (New Orleans) record experimental studies in which they observed the effects on the leucocytes of animals of the toxic products of certain bacteria recovered from the faeces and blood of agranulocytic patients They found that depression of the granulocyte counts can be readily produced by the toxins of various bacteria, their results indicating that if agranulocytosis is an infection it may be caused by more than one organism

A somewhat unusual case is described by GOADBY, WORSTER-DROUGHT, and DICKSON (London), in which meningitic symptoms occurred with changes in the cerebrospinal fluid The Lange reaction was of marked 'paretic' type, with slight but distinct increase in the total protein and a trace of globulin, suggesting a chronic infection of the central nervous system

Pentnucleotide Therapy.—A drug which has recently been found to be very efficacious in this condition is *Pentnucleotide* The property possessed by nucleic acid of producing leucocytosis has long been known Nucleic acid on alkaline hydrolysis produces pentose nucleotides, and the product in question is prepared by such a process from the nucleic acid of yeast It consists of the sodium salts of four nucleotides and is obtainable as an 8 per cent solution The dose is 10 ml by intramuscular injection twice daily for four days and thereafter once daily until definite improvement results It appears that in most cases clinical and haematological improvement does not begin until about five days after treatment has begun, after that improvement is steadily maintained

A number of early reports—mostly from America—were reviewed in these pages a year ago (PRESCRIBER, 1935, Feb, 67) Since then numerous reports, mostly favourable, have appeared

BOULTON (Bristol), being unable to obtain pentnucleotide, gave at first sodium nucleinate Later he was able to give pentnucleotide, but it was too late and the patient died The case was very severe and Boulton doubts if pentnucleotide would have effected recovery had it been given earlier DORRANCE (Quebec) also reports a case in which this drug failed to bring about recovery The case was one of chronic benign neutropenia of four years' duration, influenced adversely by pregnancy, finally culminating in abortion and agranulocytic angina (malignant neutropenia) with the usual rapid course There was an accompanying streptococcic septicaemia

Other cases occurring abroad may be briefly summarized SUZMAN (Johannesburg) describes two cases, one of which was treated with pentnucleotide Both cases were very severe and both were fatal WALKER (Sydney) reports six cases Pentnucleotide was

not available and other remedies had to be employed, such as blood transfusion, neoarsphenamine, x-rays, etc Three of his patients recovered and three died HUGHES (Penang) describes a case showing severe leucopenia and granulocytopenia There was no history of amidopyrine Necrotic ulcers were present on the gums, from which *Streptococcus haemolyticus* was isolated In the absence of pentnucleotide, scarlet fever antitoxin and sodium nucleinate were administered, and the patient recovered JEHN (Neumark) describes the case of a patient aged 77 who suffered from bleeding of the gums associated with a blood count showing severe anaemia, agranulocytosis, and thrombopenia Two intramuscular injections of pentnucleotide caused the haemorrhage to cease and the blood picture promptly improved, though the injections were followed by convulsions EISENSTÄDT (Berlin) reports a case of agranulocytosis and pure lymphocytosis which was promptly cured by treatment with pentnucleotide These are only a few typical cases out of many reported in recent literature

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TREATMENT OF MIGRAINE.

THE migrainous patient has always been a suitable subject for investigation, and treatment has varied in accordance with the results of research At one time the condition was regarded as a manifestation of allergy, and numerous offending foods were investigated, such as milk, eggs, wheat, fish (especially sea shellfish), pork, chocolate, nuts, etc Several authorities have discussed the importance of the hereditary factor, especially the possible transmission of sensitivity Ophthalmic surgeons are still divided in their opinion regarding the importance of eyestrain as a factor Many believe that an attack can be precipitated by eyestrain, while others find that notwithstanding careful correction of refractive errors the patient is not helped The condition has also been studied in relation to diseases such as epilepsy, paroxysmal tachycardia, pituitary enlargement and other endocrine disturbances, and disorders of the vegetative nervous system The rarer manifestations of migraine, cerebral and abdominal, have also been reported on and include permanent hemianopia and cerebral oedema

Some authorities connect migraine of local origin with cervical neuralgia and fibrositic nodules, a condition that responds to massage and ionization One case of definite hereditary migraine developed severe cervical neuralgia during and for some time after pregnancy There was no optic neuritis and no definite enlargement of the sella turcica When the neuralgia ceased the ordinary attacks of migraine returned There was no evidence that the attacks were of the endocrine or menstrual type

In a general article on the subject, CRITCHLEY discusses treatment from various aspects, such as the severity of the attack, the type and position of the headache, and the precipitating factors, if any In addition to the usual complete neurological examination, he lays stress on auscultation of the skull with a view to the diagnosis of blood vessel tumours such as aneurysms and angiomata As regards drug treatment, phenobarbitone, half a grain twice daily, is useful, but it does not suit every one Where an endocrine factor may be at work, dry thyroid, $\frac{1}{10}$ grain may be given thrice daily Tablets of glyceryl trinitrate, B P , were used at one time, but they are now largely replaced by the barbiturates When the migraine is of biliary origin, Carlsbad salts followed by a copious draught of hot fluid in the morning, or duodenal intubation using a 30 per cent solution of magnesium sulphate, may be employed Menstrual migraine may be treated with ovarian or placental extract

Sometimes an impending attack can be shortened if measures are taken promptly When after sleeping too long the patient has a feeling of discomfort followed by headache he should remain in bed for some time and take a draught containing bromide, acetylsalicylic acid, or caffeine, singly or combined For chronic ill health in the migrainous subject, tonics of the strychnine class are

recommended. Attention to diet and change of air are beneficial, and spa treatment at Harrogate or Llandrindod Wells may be recommended.

The use of ergotamine tartrate is discussed by LENNOX and VON STORCH (Harvard Univ.), who employed this drug in a group of 120 cases. The initial trial resulted in abrupt and complete relief from the headache in 107 of these patients. Nineteen patients used ergotamine for more than a year, and all but one obtained relief each time it was used. In some patients a tendency to more frequent recurrence or the appearance of unpleasant symptoms limits the use of the drug. The best method of administration is by intravenous or subcutaneous injection; by the mouth it is relatively ineffective. The beneficial action is specific in migraine, as headaches from other causes are either not benefited or are made worse. Ergotamine raises the blood-pressure, and care should be exercised in administering it to patients with arterial disease; the possibility of ergotism also must not be overlooked. The usual dose is 0·5 mg. ($\frac{1}{120}$ grain), but for some patients half or even one-third of this dose is sufficient. By the intravenous route relief is experienced in 15-30 minutes; the subcutaneous route requires 45-90 minutes, but there is less likelihood of nausea, vomiting, or muscle pain. In milder cases oral administration is often sufficient. From two to five tablets of 1 mg. ($\frac{1}{60}$ grain) may be given when the headache begins, followed by one or two at hourly intervals until 9 or 10 mg has been taken and relief has been obtained. While the drug is invaluable in aborting individual attacks, its use should not take the place of efforts to find the cause of the condition.

Treatment by means of calcium has many supporters. It was introduced by Untersteiner of Salzburg, who found it to be efficacious in epilepsy. For migraine he gives 15 gm. daily of the double lactate of calcium and sodium, combined with small doses of phenobarbitone, amidopyrine, and caffeine citrate, which are gradually decreased and withdrawn as the attacks become fewer. P. A. H.

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Puerperal Fever: Antistreptococcal Serum.—L. COLEBROOK (London) concludes from experience at Queen Charlotte's Hospital that antistreptococcal serum not only has no curative effect in puerperal fever, but that it may sometimes prove harmful.—*Lancet*, May 11, '35, p. 1085.

Cirrhosis of the Liver: Insulin.—WALKER and WOOD report a case of cirrhosis of the liver which showed marked improvement on treatment with insulin and a high carbohydrate diet. Abdominal paracentesis, necessary thirty-two times, was discontinued altogether. —*J.A.M.A.*, July 20, '35, p. 196.

REVIEWS OF BOOKS.

Vitamins in Theory and Practice. By Leslie J. Harris, Sc.D., D.Sc. Pp. 240. (Cambridge Univ. Press. 8s. 6d.)

This book is based on a series of lectures delivered by Dr Harris at the Royal Institution in 1934. It is written in 'popular' style, enlivened with gleams of humour, and illustrated with effective and helpful plates and drawings The whole story of vitamins is told, from their discovery —or rather their evolution, for vitamin deficiency was recognized long before the word was coined—through a description of the vitamins now known, to the application of the science of 'vitaminics' to practical dietetics. It is a fascinating story, and well told by the author—indeed as an easily assimilated exposition of the subject it is among the best we have seen. T. S.

NEW PATHWAYS IN MEDICINE is the title of a public inaugural lecture delivered in the University of Liverpool by Professor Henry Cohen, M.D., F.R.C P, and published for the University Press by Hodder & Stoughton at one shilling. It reviews in a pleasing and popular manner the more recent developments of medical science such as have been presented in the pages of THE PRESCRIBER during the past few years. The booklet is well printed and produced and furnishes interesting reading.

The Annual Report of the LEBANON HOSPITAL for mental diseases at Asfurieh, near Beirût, Syria, is an interesting document. Certain extensions recently put in hand are now in great part completed, but in view of the present political situation the money allotted to their equipment must be held in reserve as a local emergency fund There is thus great need for further funds, so that the buildings may be equipped and taken into use. Donations will be gratefully received by the General Secretary, Miss Hilda Fox, Drayton House, Gordon Street, London, W.C.1.

Salicin, B P., the crystalline glycoside obtained from the bark of various species of willow and poplar, still seems to hold its own against the many synthetic drugs used for similar purposes Its uses in influenza, in rheumatism, and in skin diseases are set forth in a pamphlet SALICIN recently issued by the makers. Salicin is manufactured in Great Britain by three firms only: J. F. Macfarlan & Co, 109 Abbeyhill, Edinburgh; T. & H Smith Ltd, Wheatfield Road, Edinburgh; Whiffen & Sons Ltd, Carnwath Road, Fulham, London, S.W 6; any of these firms will supply samples and literature on request

An informative pamphlet on CLAUDEN comes from Medical Laboratories Ltd, 40 Pall Mall, London, S W.1, the agents for this product. Clauden is a greyish-brown amorphous powder obtained from pulmonary tissue and has been introduced as a haemostatic having a very rapid thromboplastic action. To judge from the bibliography it has been widely and successfully employed on the Continent as a treatment for all forms of haemorrhage. Clauden is supplied in four forms: solution for parenteral use or for irrigation, tablets for oral administration as a prophylactic, powder for dusting on wounds, and dressings such as gauze, etc. Its action and uses are clearly set forth in the pamphlet, which is free to the profession. The cover bears a very striking illustration

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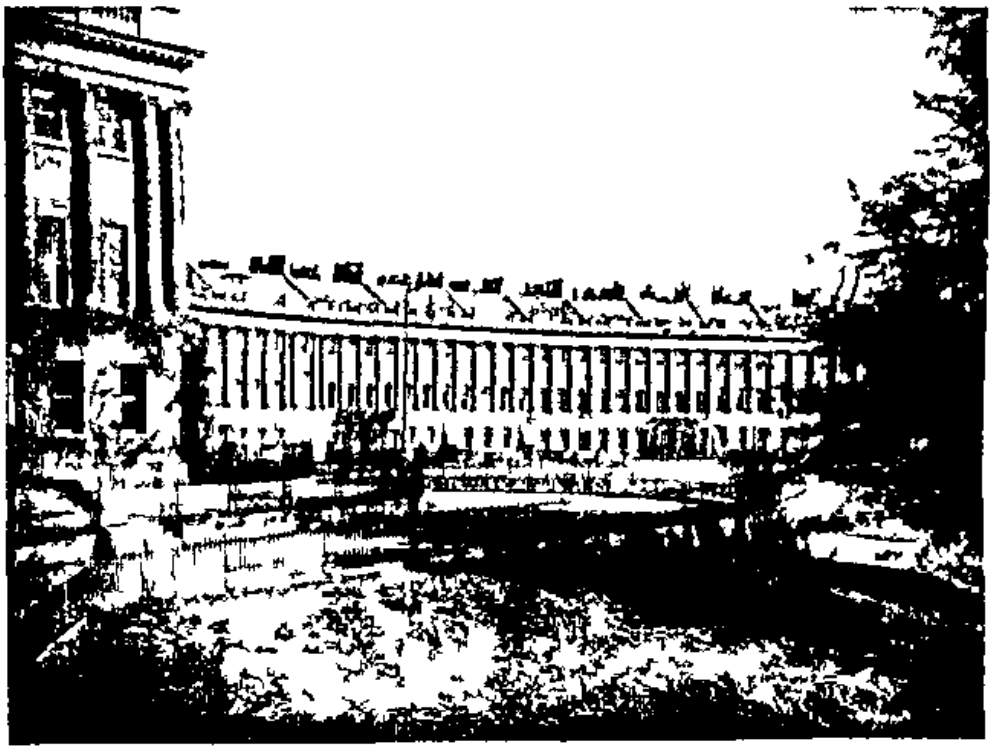
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BRIDGE OF ALLAN
THE PUMP ROOM AND
SUN LOUNGE



STRATHPEFFER SPA
PUMP ROOM AND BATHS.

ENGLISH SPAS



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Ba h

THE ROYAL CRESCENT BATH
Built by Joh Wood the younger in 1769



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The Prescriber.

TWENTY-SECOND ANNUAL NUMBER ON SPA TREATMENT

Vol. XXX. No. 3. EDINBURGH, MARCH 1936. SERIES No. 354.

SPA TREATMENT IN THE BRITISH ISLES

SINCE the institution of our Annual Spa Numbers twenty-two years ago a remarkable development has taken place in the spas of these islands. Spa treatment has evolved from a mere empirical 'drinking the waters' to a definite method of treatment, including a scientific study of climate, environment, and physical therapy, and a more rational outlook on the effects of waters and baths. Medical hydrology, in short, has come into its own and is being studied and practised as a distinct branch of the healing art.

British Spas.

A most gratifying feature of this development has been the improvement of our own British Spas. During these two decades not a year has passed but something new has been recorded at one or other of them. We have no wish to belittle the spas of Europe and elsewhere, indeed we are ready to admit that in some cases a course of treatment at, say, Nauheim or Pistany is to be recommended, but for the great majority of cases occurring in these islands it must be emphatically stated that all the necessary treatment can be had without crossing the Channel. Our Federated Spas alone offer a variety of climate sufficient to meet most cases, while the saving in time and expense is an advantage that is fully recognized by medical men and their patients.

Scottish Spas.

The spas of Scotland are deserving of more than passing notice. In an article in this issue the Editor describes visits paid last summer to Bridge of Allan and Strathpeffer, both of which spas deserve consideration by physicians. These spas are well equipped and each has an individuality that appeals in certain cases. For patients at not too great a distance they offer all the amenities of first-class health resorts.

Choice of a Spa.

It is pointed out by Dr Aldred-Brown in this issue that the key-note of all spa treatment is the regulation of disordered function. For this purpose almost any spa can furnish suitable treatment, consequently the choice of a spa is essentially a question of climate. Some spas are bracing and tonic, some are mild and sedative, while others again lie between these extremes. The patient's condition must be the guide, and in this respect the Descriptive List of Spas in the present issue should prove helpful.

B.H.R.A.

The third annual report of the British Health Resorts Association covers the work of that body to September of last year. The chief activity of the Association has been the organization of conferences, of which two have been held during the year, at Buxton and at Margate. Both conferences were highly successful in bringing to the notice of the profession and of the public the value of our health resorts from the medical standpoint. The Association's Handbook, which is issued annually, is under the able editorship of Dr Fortescue Fox. The work of the Association is not restricted to spas, but embraces seaside and climatic resorts of all kinds. Like all bodies of this description, its early work is hampered by want of funds, and subscriptions are earnestly desired. Medical men interested may obtain full particulars from the Secretary, Dr Alfred Cox, *O.B.E.*, 199 Piccadilly, London, W.1.

I.S.M.H.

Another body concerned in the study of spa treatment is the International Society of Medical Hydrology. This is a purely scientific organization: it is not concerned with publicity as such, and it is international in character. Its membership embraces medical men and scientists from almost every country in the world who meet each year in a different country and discuss various aspects of spa treatment. Apart from the stimulus thus given to the scientific study of waters and baths, this Society has been instrumental in bringing together in friendly conference men of all countries and nationalities having a common interest, in itself an achievement of no small value. The Society's organ, the *Archives of Medical Hydrology*, is published four times a year. The address of the General Secretary is 109 Kingsway, London, W.C.2.

ORIGINAL COMMUNICATIONS.

Conditions Amenable to Spa Treatment.

By G. R. P. ALDRED-BROWN, B.A., M.B., B.Ch.Oxf.,
Senior Physician, Royal National Hospital for Rheumatic Diseases, Bath

FOR a spa to be of maximum service to the sick members of the community it must fulfil several criteria. It must have a salubrious climate with plenty of sunshine and be sheltered from the prevailing winds. There must be also :—

(1) An efficient train service to that spa from all parts of Great Britain.

(2) Comfortable hotels with tariffs to suit all pockets. These hotels must be close to the bathing establishment or there must be special transport facilities for the patients to and from the baths. Further, each hotel should be equipped with a dietetic kitchen and able to issue its own menu to a patient on a special diet.

(3) Level promenades for exercise and facilities for short local excursions.

(4) Amusements such as concerts, operas, theatres, and cinemas of a high standard, so that the leisure time of the patients may be passed pleasantly. It will be noted that I have excluded a casino from my list of amusements. I am definitely against late nights for patients undergoing spa treatment. It will be found that these people invariably do badly. This point is well illustrated by the fact that Pistany, on the insistence of its spa physicians, abandoned its casino.

(5) An efficient team of physicians, surgeons, radiologists, bacteriologists, biochemists, etc., with well-equipped laboratories. Further, first-class nursing homes must be available.

(6) Lastly, but most important of all, a health-giving natural spring. It is true that natural water springs abound the world over, some hot, some cold, but only a few can hold real claim to therapeutic properties. Even now with all the vast amount of work that has been done, especially on the Continent, on the composition of natural waters and

their reaction on the body, much of hydrology still rests on empiricism. But it is inconceivable that such natural waters at spas that have been used generation by generation, even by the Romans and the people before them, should be lacking in health-giving properties. It is said truly that you can fool some people some of the time, but you can't fool all people all of the time.

Having thus enumerated the attributes of a spa, it is, in order to understand why spa treatment proves so successful in the treatment of various disordered conditions, necessary to inquire just what a spa offers to the patient seeking treatment there.

First of all there is the psychological element—change of environment, freedom from domestic worries, different climate.

Secondly, what amounts to a second opinion is obtained about the case. The spa physician, helped by the clinical notes of the practitioner, is able to bring an unbiased judgment to bear on the case.

Thirdly, at the best spa there is the provision of an up-to-date bathing establishment where every variety of hydrological treatment with the natural waters may be given, whether it be simple immersion baths with or without undercurrent douches to effect a powerful massage, hand-massage douches under jets of water, vapour baths, whirlpool baths, or colonic irrigations, etc. Further, there is provision for all ancillary treatments such as mud baths or packs, dry massage, etc., together with a fully equipped electro-therapeutic department. In addition there is provided a thoroughly trained and intelligent staff of bath attendants. British spas are fortunate in this respect, the work attracting the desired type of attendant.

Lastly, but not least, as a routine measure there is ingestion of the natural waters. The importance of this should not be underestimated. It is true that doubt is often expressed whether these natural waters when drunk have any efficacy, but experiments have shown conclusively that ingestion of such waters has a profound effect on the system.

What then are the disordered conditions for which spa treatment is most suitable? Pre-eminently one must place disorders of metabolism. It has been shown again and again how these natural waters react on the metabolism

of the individual, and one has in these waters therapeutic weapons whereby, with a judicious interplay of prescribing, either an increase or a decrease in metabolism can be effected.

Thus spas should be looked upon essentially as depots where physiological aberrations may be corrected. *The keynote of all spa treatment is the regulation of disordered function.*

Too much stress has been placed on the individuality of any one spa to cure this or that complaint. While it is true that certain waters may contain substances in solution that have a specific action on this or that organ of the body, every spa that is worthy of its name, as a spa fulfilling the criteria I have already enumerated, should be in a position to deal adequately with the regulation of disordered function.

The choice of a spa is much more a question of climate. In the winter months there can be no doubt that spas with a mild climate should be chosen, whereas in spring and summer all spas are in season.

By what means do spas secure the regulation of disordered function? They do this in two ways. Firstly by the daily ingestion or drinking of the waters. This is really important, although perhaps not sufficiently realized by the medical profession. Most spas have a mineral water which on ingestion is diuretic. Some have high calcium salts which mitigate or prevent the precipitation of urate deposits in the body or may even act as solvents of the already precipitated urates. Others have radium and/or radon substances in solution which in some way, at present undetermined, act on the metabolism of the individual. It is interesting to note in this connexion that the physiological results obtained by natural radioactive waters are not obtained by ordinary water artificially radioactivated.

Secondly by balneological treatment. This may be divided into (*a*) eliminative, (*b*) sedative, (*c*) stimulative, (*d*) special methods.

(*a*) Eliminative methods (*e.g.*, sweating treatments).—Under this heading comes a large group of disease processes amenable to spa treatment. It must be remembered that the skin is an organ of touch, excretion, and secretion. Further, it is reactive to every external impression and

especially to temperature. When the threshold for these normal impressions is lowered, physiological equilibrium is disturbed and illness is the result. A few examples of such conditions would include gout, arthritis (including osteoarthritis), fibrositis, obesity.

(*b*) Sedative methods (*e.g.*, immersion baths).—Such baths may be hyperthermal, that is, given at a higher temperature than that of the body. Their chief use is for the relief of pain and the relaxation of spasm in muscles. In this connexion I would point out that in all forms of arthritis, whether rheumatoid or osteo or spondylitis, groups of muscles are in constant spasm, and the wasting of the muscles that accompanies the diseased joints is not the wasting of disuse but wasting from the fatigue of over-use in the constant spasm. Heat by its sedative action on these overactive muscles gives them a very requisite rest. It is true that various forms of electrical heat will serve this purpose, but the advantages of a hyperthermal immersion bath are very real, as in addition to the heat effect one obtains the pressure effect of the water, and at some spas the inhalation of the natural radioactive gaseous vapour at the same time.

Or the baths may be thermal baths, that is, given at a temperature similar to that of the body. By such means stimulating influences on the skin are rendered minimal; the rate of the heart is thereby slowed and the peripheral circulation is equalized.

Examples of diseases that benefit from these methods are the anxiety neuroses, mental excitation, and especially cases of high blood-pressure. Many skin complaints such as psoriasis, eczema, etc., disappear after the application of sedative mineral water baths.

(*c*) Stimulative methods (*e.g.*, subaqueous massage douche; Scotch douche).—Such forms of balneological treatment, either by the mechanical force of fine jets of water or by artificially alternating the temperature of the water, act as powerful stimulants to the skin, thus increasing metabolism and having a tonic effect.

Conditions amenable to such methods include debility after acute illnesses, nervous debility, neurasthenia, muscular rheumatism, sufferers from the chilblain circulation, cases of hypotension, etc.

(*d*) Special methods (*e.g.*, re-educative movements, colonic lavage).—Re-educative movements are carried out

to the very best advantage when the part or parts to be re-educated are kept under hyperthermal water and where the volume of the water is such that a pressure effect is obtained. In such a medium voluntary exercise can be taken with a minimum of fatigue and strain since the hyperthermal water both supports the limbs and relaxes spasm. Under the same conditions manipulation is at its easiest and safest.

Conditions occurring under this heading are all forms of muscle spasm and/or muscle wasting occurring in every form of chronic arthritis, including spondylitis and all types of gout; the after-treatment of fractures and injuries; paralysis whether flaccid or spastic.

Colonic lavage with a natural hot mineral water is ideal therapy in such conditions as chronic constipation and alimentary toxaemia arising from intestinal stasis, tonic hardening of the colon, hepatic stasis, diverticulitis, mucous colitis, and chronic inflammatory conditions of the colon.

It must be realized that I have made no attempt to tabulate all the conditions amenable to spa treatment. Such examples as I have given are fairly obvious; there are many other conditions which at first sight may be deemed unsuitable for spa treatment, but which, however, do remarkably well at a spa, the reason probably being that the underlying metabolic factor had not been appreciated.

In conclusion, I wish to emphasize also the *preventative* side of spa treatment. It is the experience of all spa physicians that the best final results are obtained in those cases where patients who have been relieved of their symptoms at a spa are prepared to return for further spa treatment at a later date, say after six to twelve months, according to the nature of their complaint, even though they may be symptom-free at that later date. An excellent example of this is provided by the common complaint fibrositis; I include in this group forms of it labelled lumbago, myalgia, and conditions where fibrositic thickenings around nerve sheaths give rise, for example, to sciatica or brachial neuritis. One finds that those patients whom one has advised through their family physician to return after a certain lapse of time and who do adopt this course are kept entirely free from all symptoms of fibrositis, whereas others who for various reasons do not return nearly always become victims of the malady again.

THE BRITISH SPAS REVISITED.

III. The Spas of Scotland.

By THOMAS STEPHENSON, D.Sc., F.R.S.E.,
Editor of THE PRESCRIBER

COMPARED with England and Wales, Scotland is relatively poor in mineral waters, though what she lacks in quantity she fully makes up in quality. Her two spas, Bridge of Allan and Strathpeffer, have all the attributes of first-class health resorts, and can take their place alongside any of the well-known spas south of the Border. A number of isolated wells exist throughout the country, of which St Bernard's Well in Edinburgh and Pitkeathly springs in Perthshire may be cited as examples, and Moffat has two mineral wells in its vicinity, but none of these places has the character of a spa. Certain rumours were current in the early part of last year to the effect that efforts were being made by Moffat to reorganize and develop the mineral wells on the lines of Bridge of Allan, but inquiries of the civic authority there elicited the information that no such development is contemplated in the near future.

In previous articles in this place (see PRESCRIBER, Mar. *1932, p. 93*; Mar. *1933, p. 79*) my visits to the spas of England and Wales have been recorded, and to make the record complete it was necessary that I should visit those of Scotland. Accordingly a matter of ten or twelve days last summer was devoted to visiting Bridge of Allan and Strathpeffer. Through the courtesy of the officials I was enabled to make a full inspection of the spa establishments; to drink the waters, sample the treatments, and generally to take an impression of both places. Bridge of Allan and Strathpeffer have great potentialities as spas, and both are doing their best to develop their resources. The two places differ in many respects: in situation, in climate, and in waters they are distinct, being complementary rather than competitive.

Bridge of Allan.—The situation of Bridge of Allan makes it an ideal health resort. It lies on the southern slopes of the Ochil Hills and is picturesquely situated 'on the banks of Allan Water.' It overlooks the wide

fertile 'carse' watered by the serpentine windings of the Forth, above which stands Stirling Castle on its solitary rock like a guardian of the district, with the Abbey Craig carrying its rough-hewn monument to William Wallace posted like a sentinel on the other side. Stirling Bridge lies between. The district is the cradle of Scottish history: five battlefields can be seen from the Wallace tower. It is difficult to realize that this district, now so peaceful and so fertile, should have been once the scene of so much bloody conflict: the prospect to-day is serenely pastoral and suggests happiness and contentment. Far over to the west are the hills of Lomondside, standing as a barrier against the moist winds of the Atlantic—too far away to intercept any of the sunshine. Indeed the town has a purely southern aspect and gets all the sunshine available the year round, while being completely sheltered from the north and east. Consequently its climate is mild and equable: when Edinburgh is shivering in east winds or Glasgow is bathed in fog, Bridge of Allan is smiling and spring-like. Yet it is only an hour by rail, and a little more by road, from either of these cities. A quiet retired spot, admirably suited to the convalescent, yet within ten minutes bus-run of Stirling, it has all the makings of a first-class spa and only needs to be known to be sought after.

Another of its advantages is its position as a motoring centre. It is the gateway to the Highlands. In less than half an hour one can reach Callander, and a little farther on the country made famous in the *Lady of the Lake* and *Rob Roy*, or one can go round by Aberfoyle and the Lake of Menteith, with its associations of Mary, Queen of Scots. Other good runs are available, and the convalescent can have an afternoon drive of several hours in glorious and interesting country.

The spa establishment is in the grounds of the Allan Water Hotel. It is connected with the hotel by a covered way, but the front entrance is open to the public. The hotel is located in a quiet spot, some hundred yards or so back from the main road and away from the noise of its traffic. The covered way allows hotel residents to visit the pump room before breakfast and to drink the water in the sun lounge facing south.

The Spa was reconstructed in 1930, and the new establishment, then taken over by the Allan Water Hotel, was formally opened in October of that year. The pump

room was remodelled on modern lines and a commodious and comfortable vita-glass sun lounge was added. A spacious lawn in front is available in summer weather. At the back of these premises there is now a large annexe completely equipped with baths and treatment rooms, where all the most modern spa methods are available at the hands of certificated male and female assistants under the supervision of Dr Phyllis Lunn.

The mineral waters of Bridge of Allan have been known for 150 years, and recent analyses correspond very closely with analyses made over a century ago, which shows that the waters are constant in composition. There are several springs, all yielding a saline water at a temperature of 52° F. (for drinking they are heated to about 130° F.), the main features of the water being salts of calcium, iodine, and bromine. The indications for their use are many: internally they are serviceable in subacute and chronic rheumatic conditions, in gastric, hepatic, and respiratory disorders, in certain skin affections, and in convalescence. In respiratory affections they have been administered as a spray with considerable success, while as baths and douches they have several applications. Taken internally the water has a slight aperient effect and a marked diuretic action. It is by no means unpleasant to the taste.

The impression conveyed by the visit was distinctly favourable. Bridge of Allan is a complete little spa; in climate, situation, and accessibility it is ideal, while the spa establishment itself is thoroughly up to date and is well managed. Physicians would be well advised to write to the Spa Director for full particulars of the waters and treatments.

Strathpeffer.—In many respects Strathpeffer is the antithesis of Bridge of Allan. It lies in the midst of high bare mountains in the very heart of the Ross-shire highlands, surrounded by the wildest possible scenery, yet itself the strath of the Peffery is a green and fertile valley enjoying a very favoured climate by virtue of these very mountains which serve as a weather-screen. Strathpeffer town is a cluster of grey stone houses nestling at one end of this green valley, which is dominated by the majestic Ben Wyvis 3500 feet above.

Strathpeffer is a long way from Edinburgh—188 miles—and the journey occupies some seven hours by rail, but the route runs through scenes of ever-increasing

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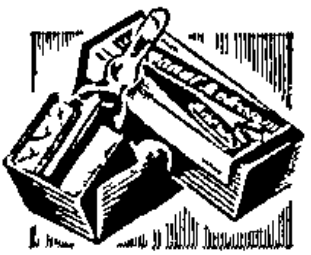
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grandeur. After leaving Perth one is soon in the Highlands, passing through Pitlochry and Killiecrankie, then over the Grampians to Kingussie, Aviemore, Strathspey, and on to Inverness. There one changes to a local train for a beautiful run along the shores of the Beauly Firth and north to Dingwall, after which the train turns west into the valley of the Peffery and finally pulls up at the little station of Strathpeffer. From the station one enters the little town—a cluster of villas and small shops, with several large hotels and a number of smaller hotels and boarding-houses. The Spa with its large glazed courtyard stands in a central position and is within a minute or two's walk of any part of the township.

The Pump Room is the 'community centre' of the town: it starts early, all except perhaps the more decrepit invalids being there before breakfast. From 8 to 9 A.M. music plays and people assemble for their 'pre-breakfast' draught of sulphur water, and the scene is one of bustle and activity. After breakfast, that is, from 11 to 1, the Spa is again active, though more quietly so. By this time the invalids are inside having baths or treatments, while the more robust are out motoring or golfing. But the Spa is still the rendezvous: people keep coming and going and the skirl of the pipes imparts a suitable atmosphere.

Strathpeffer lies in a valley—green, sheltered, and cosy. To obtain an idea of the surrounding country—the sheltering element—one must mount to the golf course, which lies on the upper edge of this hollow. The climb is not very stiff, and the climber is well rewarded, for in front of him lies a stretch of level heather-covered moorland, beyond which are the mountains of Ross-shire. A walk of about three-quarters of a mile across this moorland brings us to the farther edge, from which the view is truly magnificent. We seem to have come to the end of the habitable globe, for as far as eye can reach are wild bleak mountains to all appearance devoid of all life, animal or vegetable. Here and there the ruggedness is relieved by a mountain tarn lying in the hollow of some mountainside like a pool of ink, or perhaps reflecting the sunshine like a dark mirror. The scene is weird and uncanny in the extreme, and one can well understand how people born and bred in such surroundings believe in second sight and mountain spirits. It is a fascinating sight, and it is only the recollection that a good mile and a quarter lies between us and our hotel that tears us away from the scene.

One might imagine that with such surroundings the climate of Strathpeffer would be cold and bleak—it is exactly the opposite. So sheltered is the situation that rainfall is low and cold winds are intercepted. In summer the average temperature is only 6 degrees below that of London, while in winter it is only 1 degree lower. On the upper slopes, as at the golf course, the air is fresh and invigorating. The sunshine record is high, and in the summer months the sun rises an hour earlier and sets a full hour later than in the south of England—indeed in June there is little darkness, only a sort of twilight between sunset and sunrise. Strathpeffer is essentially a tonic spa; it is not suited to acute cases or to persons with high blood-pressure.

The waters are Strathpeffer's other asset. It has four sulphur springs in addition to a chalybeate water. The water from the Cromartie Well is particularly strong in sulphur and has no chloride ingredients. The water from No. 2 well is slightly aperient, containing magnesium sulphate. All the waters are obtainable at the Pump Room, the strong sulphur water being the most popular. The sulphur water is used in the baths, as also is peat obtained in the district. All the accessory treatments are to be had, qualified attendants being employed. For chronic rheumatic and gouty affections, for gastric and hepatic disorders, and for skin conditions such as eczema, the waters and baths are particularly suitable. Strathpeffer seems to be particularly well adapted for the over-tired brain worker: the place is very restful and at the same time the air is stimulating and bracing. Its one drawback is its distance from southern centres, but as it is a purely summer resort, and as the journey is one of continual interest and pleasure and can be accomplished from the south of Scotland in half a day, that should not detract greatly. When the invalid arrives there he is soon braced up, and the pleasant character of the environs tempts him to prolong his stay.

The spas of Scotland may be few in number, but they can hold their own with any in the British Isles. Physicians especially in the north of England and in Scotland itself should bear them in mind. In addition to suitable waters and treatments they offer a complete change of scene; they have a character of their own which by directing the brain into fresh channels of thought provides an important factor in the 'cure.'

THERAPEUTIC NOTES.

Headache after Lumbar Puncture.—According to LEMAIRE and BIOY headache following lumbar puncture can be rapidly relieved by hypodermic injection of 0·02 gm. of acetylcholine. The dose may be repeated if necessary.—*Progrès méd.*, Nov. 28, '34, p. 1871.

Malnutrition: Insulin.—A. TOW (New York) reports that insulin is a valuable aid in effecting a gain in weight in the malnutrition of non-diabetic children.—*New York St. J. Med.*, July 15, '35, p. 719.

Meningitis: Avertin.—R. E. H. SIMPSON reports two cases of meningitis in boys aged respectively 9 and 12 successfully treated with avertin. Full doses were given three or four times in each twenty-four hours.—*Lancet*, Aug. 17, '35, p. 404.

Meningitis: Lipiodol.—Two cases of localized chronic inflammatory meningitis are reported by HARROWER (Singapore). In both lipiodol was injected into the cisterna magna primarily for diagnostic purposes, and in both the symptoms were alleviated in an almost miraculous way, with complete recovery later.—*Lancet*, Sept. 28, '35, p. 715.

Phenol as Gastric Sedative.—J. C. LYTH recommends phenol in 2-minim doses as an effective means of checking vomiting and generally of relieving gastritis from whatever cause. Combined with ipecacuanha it is a useful expectorant.—*B.M.J.*, Nov. 9, '35, p. 903.

Trichomonas Vaginitis: Saline Douches.—Vaginal douching with 25 per cent. salt solution, according to L. ROSENTHAL *et al.* (Brooklyn), gives prompt relief and in most cases prevents recurrence. The effect is due to osmotic action, and is non-irritating and inexpensive.—*J.A.M.A.*, July 13, '35, p. 105.

Paroxysmal Tachycardia: Acetylcholine.—A. B. STENHOUSE (Oxford) reports a case in which increasing doses of acetylcholine (25, 50, and 75 mg. subcutaneously) were followed by progressive slowing of the heart-rate.—*Lancet*, Dec. 7, '35, p. 1291.

Haemorrhagic Disorders: Ascorbic Acid.—H. ENGELKES has found vitamin C (ascorbic acid) of great value in capillary haemorrhages, including essential thrombopenia, purpura infectiosa, and essential haematuria. In the last-mentioned synthetic ascorbic acid ('redoxon') was given intravenously in doses of 0·1 to 0·2 gm. as well as orally.—*Lancet*, Dec. 7, '35, p. 1285.

Ulcerative Colitis: Ascorbic Acid.—G. HETÉNYI has treated seven cases of ulcerative colitis with ascorbic acid, with good results in six. The vitamin corrects the poor diet that such persons are compelled to take. Daily intravenous injections of 0·15 gm. are given until only one motion occurs daily, when it is given every second day.—*Klin. Wschr.*, Oct. 12, '35, p. 1470.

Reactions from Gold Salts —H J Williams reports that admixture with calcium gluconate will prevent the severe skin reactions so often met with when gold salts are given for rheumatoid arthritis The contents of one ampoule of allochrysine (0 1 gm) are mixed with 10 c cm of 10 per cent calcium gluconate and injected intramuscularly In sixteen cases this injection produced no severe reaction —*B M J* , Dec 7, '35, p 1098

Congo Red in Typhoid Haemorrhage —Szirmai (Neupest) has found that in cases of typhoid complicated with intestinal haemorrhage the bleeding yields quickly to intravenous injections of congo red He gives 10 ml of a one per cent solution intravenously and repeats this every twelve or twenty four hours until the haemorrhage has ceased, and thereafter daily for a few days Given intramuscularly congo red is uncertain in its action, but intravenously it is non toxic and appears to increase the number of blood platelets and the rate of coagulation

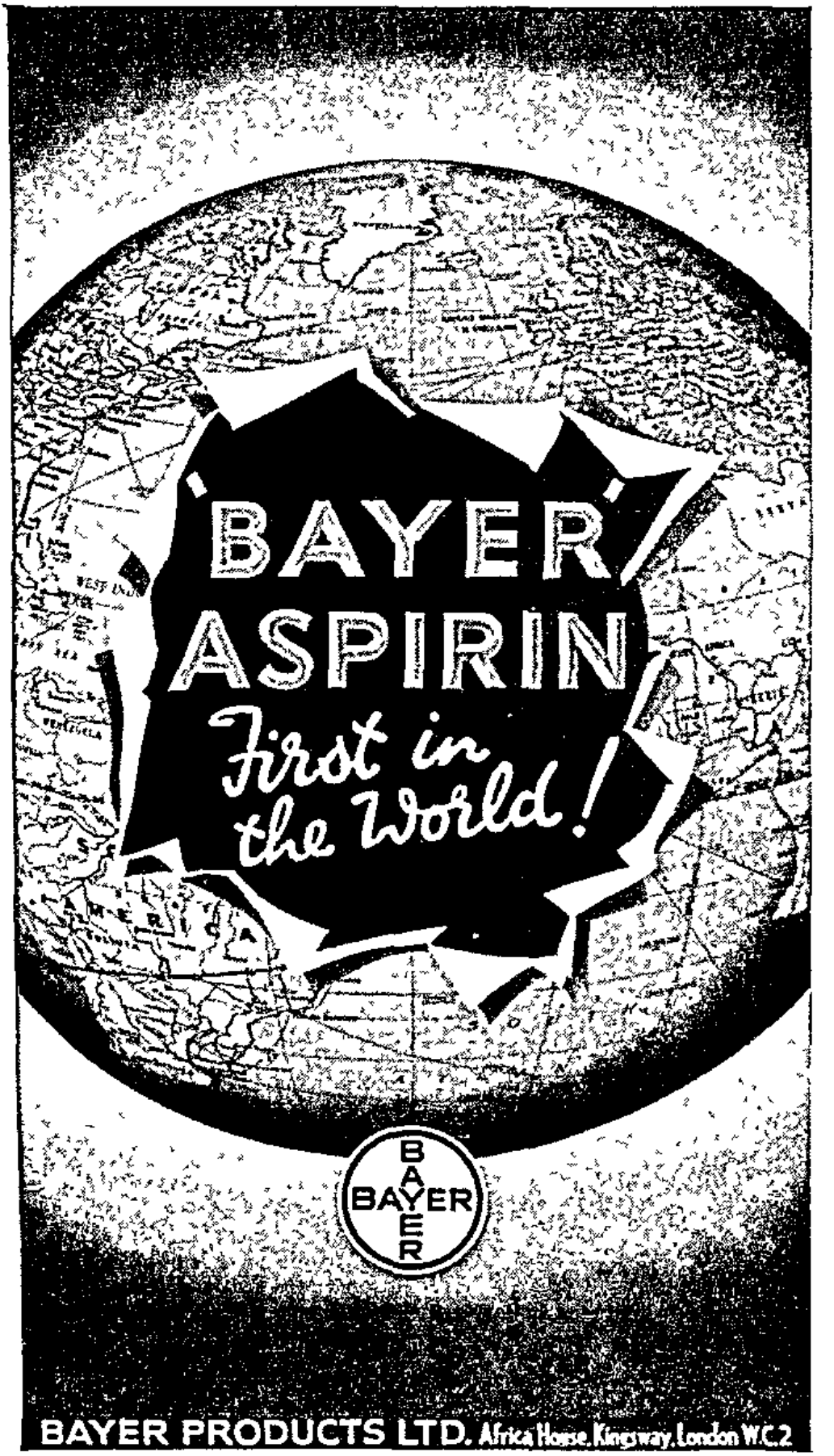
Szirmai F Ueber die Behandlung der typhösen Darmblutung mittels Kongorot *Münch med Wschr* 1935 Aug 30 1403 1404

Ergotamine in the Puerperium —Der Brucke (Brooklyn) finds that with ergotamine tartrate a mildly tonic contraction of the uterus is maintained for a longer period after delivery than with pituitary (p l) extract He gives one millilitre of ergotamine tartrate solution (0 5 mg or $\frac{1}{120}$ grain) hypodermically immediately after delivery of the placenta, and for the three following days he gives by mouth five doses daily of 0 4 ml of the same solution in order to maintain this contraction By this means the culture media in the uterine canal and the gaping sinuses are reduced to a minimum greatly lessening the chances of infection Der Brucke has used this method successfully on 400 parturient patients

Der Brucke M G Ergotamine tartrate in the puerperium *J A M A* 1935 Sept 14 867 868

Acid Treatment of Bacilluria —As the administration of ketogenic diet in the treatment of urinary infection is complex and difficult to carry out, Crance and Maloney (New York) suggest that the same result may be achieved by means of acid administered *orally They give 10 minims of nitrohydrochloric acid* (U S P 1916) in a glass of water four times daily [The average dose of the strong acid is 3 minims and of the dilute acid 15 minims , the strong acid, consisting of nitric acid 18 parts and hydrochloric acid 82 parts is definitely specified —Abstractor] It is said that, as in treatment with ketogenic diet the best results are obtained in infections with *Escherichia coli* which constitute 75 per cent of such cases

Crance A M and Maloney T W A new acid medication in the treatment of bacilluria preliminary report *J Urology* 1935 June 657 663 per *Canad Med Assoc J* Nov 35


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DESCRIPTIVE LIST OF SPAS.

In order that a list of British Spas, such as that given in the following pages, may serve as a useful guide to medical men, some method of classification is necessary. Among British Spas first place may fairly be given to those comprising the British Spas Federation, under whose rules only such places are admitted as comply with certain conditions. These rules, which furnish a useful practical definition of a first-class spa, are as follows :—

1. The possession of natural mineral waters showing on analysis a proper therapeutic value.
2. The existence of bathing and pump-room establishments of suitable size.
3. The presence in the town of medical men who devote themselves to spa practice.
4. Suitable hotel and other accommodation.
5. Treatments to be given (with certain minor exceptions) only on the authority of a physician.
6. The amenities and sanitary conditions of the town to be approved.
7. The spa to be under municipal or other approved control.
8. The provision of facilities for spa treatment must be regarded as the main activity of the spa.

The Federation aims at the provision of a certain standard of efficiency in spa treatment: before a place can justifiably be termed a 'spa' it must satisfy these requirements. The Federation fully recognizes the existence of a large number of smaller spas and health resorts—many of the latter being places of considerable importance—but until those comply with the Federation's requirements they cannot be admitted to membership as spas.

The first section of our list, therefore, comprises Federated Spas only: subsequent sections deal with other spas of more or less importance from the medical point of view.

1. British Federated Spas.

At present eleven spas in Great Britain—nine in England and two in Scotland—comply with the rules given above, and these, along with the spas of New Zealand, comprise the British Spas Federation. In the following list these spas are arranged alphabetically, with a brief indication of the character of their waters and the main indications for treatment. A detailed description of each spa follows :

BRITISH FEDERATED SPAS

Spa	*Nature of Water*	*Chief Indications*
BATH	Thermal radioactive	Rheumatism, etc
BRIDGE OF ALLAN	Saline calcium	Rheumatism, catarrh
BUXTON	Subthermal	Rheumatism, etc
CHELTENHAM	Saline	Digestive disturbances
DROITWICH	Brine baths	Rheumatic conditions
HARROGATE	Sulphur saline and iron	Rheumatism, heart affections, digestive, liver, *and skin disorders*
LEAMINGTON	Saline	Digestive disorders, etc
LLANDRINDOD	Saline	Digestive disorders etc
STRATHPEFFER	Sulphur	Rheumatism, skin disorders
TREFRIW WELLS	Strong iron	Anaemia, rheumatism
WOODHALL SPA	Bromo iodine	Rheumatism, neurasthenia skin disorders, *female complaints*
NEW ZEALAND	Various	Various

BATH, Somerset Delightfully situated in the valley of the River Avon, 107 miles from London, Bath is surrounded by hills which shelter it from the north and north east winds and at the same time allow of a variety of aspects and altitudes, varying from 60 to 750 feet above sea level, and permitting of a variety of climatic conditions The water supply and sanitation are excellent

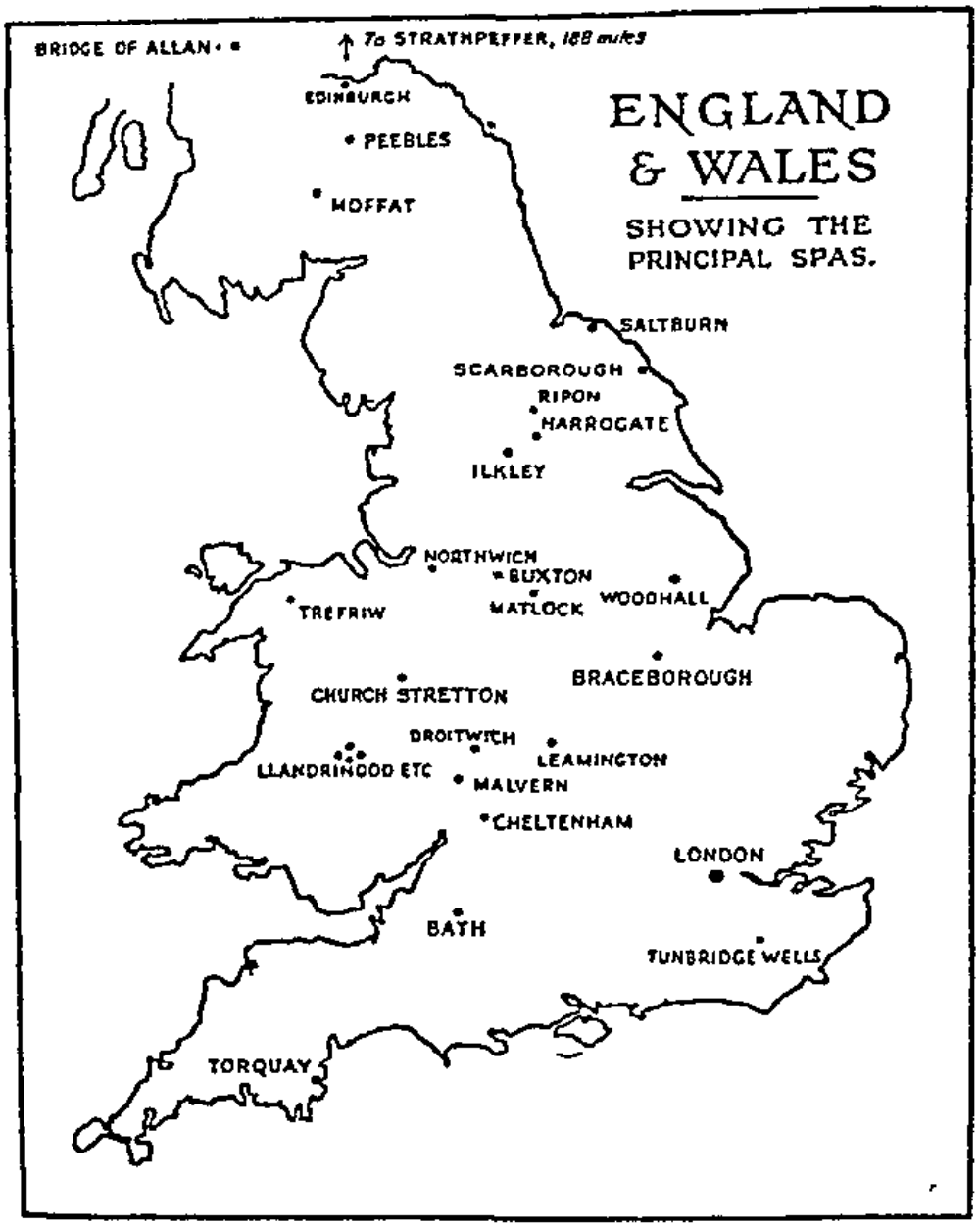
Climate—Mild, equable, sedative, specially adapted for winter treatment More bracing at higher levels Average winter temperature 42°, rainfall 26 25 inches, sunshine 1638 hours

History—The legend of Prince Bladud affords evidence of the antiquity of the Bath springs That the springs and baths were in use during the Roman occupation is beyond doubt, the original Roman bath, still extant, being open to visitors In the old-fashioned streets and crescents which still dominate the architecture, the atmosphere of the eighteenth century is maintained, though in all essentials Bath is a thoroughly modern city

Mineral Waters—Three thermal springs exist in Bath, the composition of all being very similar The waters are of a high temperature (120° F), they are the only hot springs in the British Isles, and are strongly radioactive They have a pronounced therapeutic action, the radium emanation content being largely responsible, and are specially valuable in gouty and rheumatic conditions

The waters are valuable as medical baths every variety of which is available Deep baths, douche massage, under current douching, foam treatment, whirlpool and aeration baths, and indeed every approved balneo therapeutic method, are obtainable in this well equipped establishment The high colonic douche is an important feature, the radioactive water being particularly adapted for this method of treatment A new treatment by vapour derived from the

radioactive water—the Bath 'Thermal Vapour Bath'—was recently added. Mud treatment is also employed; the mud is obtained in the neighbourhood and is mixed with the radioactive thermal water. By means of a newly devised apparatus the thermal waters are now being administered as a throat and nasal spray without any



loss of temperature. Another recently developed treatment is the deep aeration bath in which the patient, relaxed in five hundred gallons of the radioactive thermal water, is subjected over the whole surface of the body to the gentle massage of innumerable bubbles of air driven through the bottom of the bath, the limbs being exercised while in the buoyant water. Reclining baths of a similar nature are available for older or more feeble patients, and even local baths for the extremities.

A completely new electrotherapy department is being constructed

at the Royal Baths to include all the approved forms of electrotherapy Although it will form a self-contained department, the new block has been so planned as to be in direct connexion with both wings of the balneological establishment, thus enabling the treatments to be combined when required

The waters are served in the Grand Pump Room, an eighteenth-century building, handsomely and comfortably furnished and containing many of the original rout seats and other objects of interest During the spring and summer the band plays in the Parade Gardens where the mineral waters are served in the open air and a tea loggia and other amenities are provided

Season—All the year round The busiest months are from September to June, but Bath is becoming increasingly popular in the summer Amusement is provided in the form of daily concerts at the Pump Room, bands and open air entertainments in the parks during the summer, dances, theatres, etc The neighbourhood abounds in delightful walks and longer excursions

Address—John Hatton, Director of Baths, Bath

BRIDGE OF ALLAN, Stirlingshire Beautifully situated in a sheltered position at the base of the Ochil Hills, 39 miles from Edinburgh and 3 miles from Stirling, Bridge of Allan is easy of access, and has for generations been a popular health resort The district is closely associated with some of the most interesting events in Scottish history, Stirling Castle and Bannockburn are close at hand, and the beauty spots of the Highlands, such as Callander, the Trossachs, and Loch Earn, are within easy distance for motoring The neighbourhood abounds in beautiful walks, and golf, tennis, fishing and riding are available

Climate—Mild and equable, suitable for residence all the year round Southern exposure, well sheltered from north and east by the Ochil Hills

Mineral Water—Bridge of Allan has some six springs which yield a true saline water, the principal ingredients of which are sodium chloride and calcium chloride, with bromine and iodine It is odourless and very palatable, taken internally it is of value in subacute and chronic rheumatism and in some digestive disorders Inhalation of the vaporized mineral water has given some remarkable results in asthma and other respiratory disorders Its iodine content renders it valuable in glandular affections in children The mineral water is also used extensively for baths It is of value in skin affections and, as a douche, in gynaecological cases

The Spa has recently been reconstructed and enlarged, additions to the baths and hydropathic treatment rooms being a handsome vita glass sun-lounge to the south, and to the north a large hall divided into rooms devoted exclusively to electrical treatment, inhalation, massage, etc The Spa is completely equipped for both

hydropathic and electrotherapeutic treatment, and is connected by covered way with the Allan Water and Spa Hotel, having a separate public entrance for non-resident patients.

Season.—All the year round.

Address.—The Spa, Bridge of Allan. Telephone 148.

BUXTON, Derbyshire. Conveniently situated 165 miles (3¾ hours) by rail from London, and 24 miles from Manchester, Buxton stands about 1000 feet above sea-level, in the heart of the Peak district, protected from east winds by the surrounding hills and moorlands, which rise to 1800 feet. The climate is bracing and very tonic, and the porous subsoil causes the roads and turf to dry quickly after rain. Average temperature 52·5°; rainfall 48·42 inches; sunshine 1428·2 hours; prevailing winds westerly.

Mineral Waters.—The springs at Buxton are of two kinds: (1) the radioactive thermal water for which Buxton has long been famed, and (2) the chalybeate spring.

The thermal water is hypotonic, and emerges from the limestone rock at a uniform temperature of 82° F. When seen in bulk, as in the swimming baths, it is of a beautiful blue colour, with bubbles of gas (nitrogen, argon, and helium) constantly rising to the surface.

The chalybeate water is supplied in the same building. The iron is in the form of ferrous carbonate and appears to be readily tolerated and completely absorbed when the water is ingested. Used as an immersion bath, especially if aerated with CO_2, it has a useful tonic and astringent effect.

Baths.—The bathing establishments, Thermal and Natural Baths, provide every recognized form of treatment for rheumatism, including running water immersion baths, aeration baths, Plombieres douche, vapour baths, peat packs and baths, and the various forms of physical and electrical treatment, given by a fully qualified staff. A three weeks' course including every necessary treatment may be had for three guineas.

The Buxton Clinic for Rheumatism, opened in 1935, has already attracted patients from all parts of the British Isles. This Clinic, like the bathing establishments, is open throughout the year, and treatment may commence at any time. Patients are received only on the recommendation of a physician. Board and accommodation, medical advice and supervision, together with treatment, can be obtained at special reduced inclusive rates.

Buxton offers every facility for golf (two 18-hole courses), tennis, and other games. The Spa Orchestra plays twice daily during the summer, and music is provided in the Pavilion throughout the year. Excellent hotel and boarding-house accommodation is available. Places of interest in the vicinity include Chatsworth, Haddon Hall, Dovedale, etc.

Address.—For full information write to J. E. Boddington, Spa Manager, Thermal Baths, Buxton.

CHELTENHAM SPA, Gloucestershire Situated about 200 feet above sea level, 96 miles west of London, Cheltenham Spa has a westerly aspect, and is sheltered from the east by the Cotswolds Its parks, gardens, and leafy avenues give Cheltenham a character of its own The sanitary conditions of the town are good The Shakespeare country and other places of interest are within easy reach

Climate—Mild, free from extremes and from fogs, and well suited to invalids from tropical countries and to those suffering from chest diseases Average temperature 56 9°, rainfall 22 3 inches, sunshine 1691 7 hours

Mineral Waters—The waters of Cheltenham fall into four groups (1) Fieldholme, or twin salt saline, containing nearly equal proportions of magnesium and sodium sulphates, (2) Lansdown, or sodium sulphate saline, which resembles the water of Kissingen and contains sodium chloride and sodium sulphate, (3) Pittville, or alkaline saline, closely resembling that of Carlsbad or Marienbad, (4) Chadnor, or magnesium-calcium saline, which contains sulphates and calcium

A complete installation of medical baths, etc, supplies all the modern treatments The Spa is under Municipal control

Season—All the year round Social attractions include a permanent orchestra, concerts, bands, dances, etc Three 18 hole golf courses are available

Address—The Spa Manager, Town Hall

DROITWICH SPA, Worcestershire. Situated in a picturesque district of the Midlands, close to the 'Shakespeare Country,' Droitwich is 2½ hours by express from London and 20 miles from Birmingham The climate is equable, and extremes of temperature are rare

Waters and Baths—The brine of Droitwich holds in solution about 30 per cent of salts, being nearly ten times the density of sea water The swimming baths are a useful adjunct to balneological treatment the density of the water prevents the bather from sinking and allows him to practise movements of the limbs often impossible under ordinary conditions

The Royal Brine Baths Clinic was opened in 1931 for the investigation and treatment of rheumatism, and its equipment includes biochemical and bacteriological laboratories

Season—All the year round The Winter Garden adjoins the St Andrew's Bath

Address—The Baths Manager, Droitwich

HARROGATE, Yorkshire. This town is beautifully situated on the Yorkshire moors, the spa portion being in a hollow protected by higher ground It is easily reached from all directions by excellent roads and by rapid and luxurious Pullman trains, the rail journey occupying about four hours from either London or Edinburgh

Harrogate has no industry other than spa requirements. The surroundings are very picturesque; moorland and hill scenery, castles, and abbeys are within easy reach.

Climate.—Dry and bracing; tonic but not severe, the town being sheltered by the Pennine range and the uplands to the west. Average temperature 48·5°; rainfall 26·49; sunshine 1397·3 hours; the rain-bearing winds from the south-west deposit much of their moisture before reaching Harrogate. The town has a good supply of pure soft water, and is well built and admirably drained.

Waters.—Of Harrogate's eighty-eight springs, sixteen are used for internal administration, the remainder for bathing. The waters may be divided broadly into two categories: sulphur waters and iron (chalybeate) waters. Rarer constituents, such as barium, strontium, manganese, copper, and lithium, together with appreciable radium, are also present. Pharmacological research is being done on the barium content and the manganese and copper are assumed to have important catalytic properties in metabolism. Of the hypertonic sulphur waters the Old Sulphur Well is the best known. Its first effect is that of purgation; a further and important effect, recently demonstrated, is an increase in the metabolism. The other sulphur waters range from isotonic to various degrees of hypotonicity. The hypotonic waters are 'alkaline sulphur,' possessing a high ratio of alkaline carbonates to total solids. Their high sulphide content and bland character render them valuable in skin diseases where a non-irritant and bactericidal bathing medium is required. The iron waters range from isotonic down to 'pure chalybeate,' the hypotonic waters presenting a readily assimilable form of iron suitable for children and the anaemic.

The waters of Harrogate rise directly from a deep-seated granitic magma and are not dependent on any climatic or seasonal variation. In their collection and supply the best chemical engineering methods are employed, so that they are presented in the pump-rooms in a perfectly fresh and active condition. The waters are under the control of a scientific officer and analyst in whose laboratories chemical and biological work is constantly in progress. A specially equipped bathroom is devoted solely to experimental research.

A new departure is the introduction of a delightful table water, one of the springs being used for this purpose. Supplied both still and sparkling, it mixes well with spirits and other beverages, and is proving a formidable competitor to the foreign waters.

A new and excellent feature is the long 'sun walk' with vita-glass roof and sides to open or close. Adjoining the covered walk are two completely enclosed pavilions, a bandstand, and a large café. It is intended eventually to erect a new pump-room at the entrance.

Treatments.—Every recognized physiotherapeutic treatment is available. The special Harrogate treatments include baths of natural sulphur water; peat-baths with local peat; carbon dioxide effervescent baths with sulphur water by an improved and patented

method; fango packs with a local therapeutic mud, nasal sprays with natural waters All these represent the local resources of Harrogate, which are in every way as plentiful and as effective as those of continental resorts The attendants hold the certificates of either the C S M M G. or the Harrogate Medical Training School, the entire staff being certificated

Season—The amusements, entertainments, and social amenities of Harrogate are on a very high plane, the spa interest being the only industry. Waters and treatments are available all the year round The winter season (November to March) is a distinct feature, the baths, pump rooms, hotels, and amusements are all open, and prices are much lower than in the 'high season' Complimentary facilities are offered to practising medical men at all times, with reduced prices for accommodation from October 1 to July 14. A scientific booklet on the waters is supplied free to the profession

Address—F J C Broome, General Manager, Wells and Baths

LEAMINGTON SPA, Warwickshire. Royal Leamington Spa is 87 miles (1¾ hours) from London, and is situated in a beautifully wooded district, 170 feet above sea-level, on a soil of gravel and clay.

Climate—Mild and equable, the town being free from fogs and protected from winds Average temperature in 54 years, 49 5°; rainfall 29 54 inches, sunshine (October to March) 386 9 hours

Surroundings—The neighbourhood is of historic interest, Kenilworth, Warwick, and the 'Shakespeare country' being within easy reach

Mineral Waters and Treatments—The springs at Leamington Spa are saline, aperient, and diuretic Very complete baths are available—a handsome new wing was opened in 1926—and the treatments include Nauheim and other continental varieties, radioactive saline baths, Aix and Vichy douches, Berthollet, paraffin wax, radiant heat, ionization, diathermy, ultraviolet rays; also a Plombieres suite, two large swimming baths, and a Turkish bath

All departments are administered by a certificated staff under the direct supervision of the Manager and a Medical Advisory Committee A number of spa practitioners are available.

Season—April to October, winter season, November to March. Bands play in the Jephson and Pump Room Gardens and an instrumental trio plays all the year round in the Pump Room, where orchestral teas are served daily Tennis, croquet, boating, golf, and putting greens are available

Address—W J Leist, Manager, Royal Pump Room and Baths Booklets for the profession on application

LLANDRINDOD WELLS, Radnorshire (Central Wales). About 175 miles from London, Llandrindod Wells is picturesquely situated on an open plateau, 700 to 800 feet above sea-level

Climate—Dry and mildly bracing The peculiar tonic-sedative effect of the air is the result of the combination of the crisp mountain

air with the soft Atlantic breezes; these, however, are deprived of most of their moisture by the mountains to the west. Fogs are very rare. Rainfall 37 inches. The roads and surrounding country dry rapidly.

The springs are numerous and vary considerably in their composition. The waters comprise *Simple Saline*, *Muriated Sulphur*, and *Chalybeate*. The salts are chlorides, chiefly of sodium, calcium, and magnesium, with small quantities of the rarer metals. The Calcium and Magnesium Springs are rich respectively in these elements, and the Radium Sulphur Spring is definitely radioactive. The waters are of value in gouty and rheumatic conditions, in chronic digestive disorders, in liver congestion, cholecystitis, and jaundice, and in tropical and malarial anaemia and other effects of tropical residence. The baths establishment has been brought up to date and is very complete.

Season.—Nominally commencing at Easter, the season extends to the end of October. For the 'cure,' May, June, and September are the best months; for those coming from tropical countries, June to September. Good bowling greens, public tennis courts, two 18-hole golf courses, and excellent fishing are available. An excellent motoring centre in very beautiful country.

Address.—The Secretary, Inquiry Bureau, Llandrindod Wells, will send guide-book and information post free.

STRATHPEFFER SPA, Ross-shire, 590 miles from London; 188 miles from Edinburgh. Picturesquely situated in a fertile valley, 134 feet above sea-level. Climate dry and equable; average summer temperature 55·6°; average rainfall 30 inches; sunshine (summer) 6 hours daily; prevailing winds westerly. Strathpeffer is a tonic spa; the air is cool even in summer, and this is regarded as an important factor in the treatment.

Mineral Waters.—Four sulphur springs of different strengths and composition, and one chalybeate well. The sulphur water is the strongest in Europe, and, unlike that of Harrogate, contains no salt or chlorides. It is specially indicated in chronic rheumatic and gouty affections and in some skin diseases. A complete set of baths, including peat baths, foam baths, and colonic lavage, has been installed. The foam baths are given with ordinary water or with sulphur water. Sulphur inhalations and all the usual electrical treatments, also paraffin wax baths and infra-red radiation, are available.

Season.—May to October. May and June are the best months, the days being about an hour longer than in the south of England.

Address.—The Pump Room, Strathpeffer.

TREFRIW WELLS, Caernarvonshire. Trefriw is picturesquely situated in the Conway Valley, about 13 miles from Llandudno and 5 from Bettws-y-Coed, in the midst of pine woods. The climate is mild and combines sea and mountain air. Fog is unknown.

Mineral Waters—The waters of Trefnw Wells are unique, being a highly concentrated natural chalybeate The iron is in the form of ferrous sulphate, and the smallness of the dose is a distinctive feature In addition, the waters contain magnesium, calcium, aluminium, and silicates There are two springs, both similar in character.

The water is clear, with a slightly acid reaction and a pleasant ferruginous taste The dose is half to one ounce, and the water is readily assimilated and causes no gastric disturbance The waters are dispensed at the Pump Room and Baths They are of undoubted value in anaemia, in chronic skin troubles, and in rheumatic diseases generally The effect of the water is enhanced by its use in the form of warm immersion baths which are exhilarating in effect, the astringent nature of the water precluding any possibility of resultant chill The duration of the bath treatment is from two to four weeks

An important feature of this spa is the bottling and supply of the waters for home treatment The water comes from the wells through pipes direct to the bottling machines and is run into one ounce non-actinic phials, which are sealed hermetically by a special process The water in the bottles is thus exactly as it comes from the well, and the method of bottling keeps it unimpaired for an indefinite period A supply of the phials for seven weeks' treatment at home is sent to any address for 42s post paid The internal treatment may therefore be efficaciously prescribed to patients at home, and a visit to the Spa is rendered necessary only when the baths are desired

Remarkable results have been obtained in cases of rheumatoid arthritis from a protracted course of internal treatment, which is easily provided by means of the home treatment

Season—Treatment available all the year

Address—C Adamson, Manager, Pump Room and Baths, Trefnw Wells, North Wales (Medical booklet and literature free)

WOODHALL SPA, Lincolnshire Distant 134 miles (3 hours by rail) from London, this spa is situated in moorland country, about 20 miles inland, on a deep sand and gravel subsoil There are no gradients, and owing to the surrounding woods it is warm and sheltered in winter, cool and shady in summer

Climate—Dry and bracing, the air is charged from the pine woods in and around the Spa Average temperature 48 36°, rainfall 20 39 inches (about the lowest in England), sunshine 1637 9 hours

Mineral Water—The Spa water is hypertonic, and contains potassium iodide and bromide, sodium and calcium chlorides, magnesium and sodium sulphates, and a trace of iron The water has a sedative effect and is useful in rheumatism, gout, arterio-sclerosis, neurasthenia, and skin diseases Internal douches of the waters have proved of great value in diseases peculiar to women

The Baths are open all the year round and all forms of hydro-

logical and electrical treatments are given. They are situated in over 60 acres of wooded grounds which include the famous Petwood Gardens. Numerous summer-houses and shelters are provided and the Spa may claim to be one of the beauty spots of England.

Woodhall aims at being restful and recuperative, and its rural characteristics are jealously preserved. Its golf links are, however, among the best in England, and there are first-class hard tennis-courts and a modern swimming pool in the Royal Jubilee Park recently opened.

Address.—Tariff and illustrated brochure on application to the Spa Director, Woodhall.

NEW ZEALAND. No country in the world is richer in thermal springs than New Zealand; indeed the North Island alone produces more hot mineral water than all the rest of the British Empire. These waters are of very diverse character, and it is only within the last thirty-five years that a serious attempt has been made to develop them along scientific lines. Rotorua, Te Aroha, and Hanmer are under Government control and are fully equipped in accordance with European standards, while numerous smaller health resorts, such as Helensville, Waiwera, and Kamo, have been developed by local enterprise and have baths and hotel accommodation.

The attractions of a trip to New Zealand, to those who are not too closely bound by considerations of time and money, are very great. The climate of New Zealand is delightful, while the interest attached to the country itself, its geysers, fiords, mountains, and Maori villages furnishes that complete change of scene so beneficial to the invalid.

Rotorua. This is the chief place in the thermal district, situated in the North Island about six hours by rail from Auckland, at an elevation of about 1000 feet. It has been laid out and fully equipped on the European model, with baths, treatments, etc. It has numerous springs, the waters of which may be divided into acid sulphur waters and alkaline sulphur waters. The acid waters are used for baths, the alkaline waters both for baths and for drinking. The hot mud springs and volcanoes of the district furnish excellent mud baths.

Te Aroha is a quiet spa lying south of Auckland in the North Island. Its waters are of three types: thermal alkaline, cold chalybeate, and magnesia; the first of these have a character of their own.

Hanmer. The springs of Hanmer are in the South Island, 93 miles from Christchurch. Its waters are sulphuretted saline with sodium borate and lithium. They are more suited for baths, and should be drunk only in small doses and under medical supervision.

A full account of the springs and their waters will be found in *The Hot Springs of New Zealand*, by A. S. Herbert, M.D. (Lewis, 15s.). Information regarding travel, etc., can be obtained at the Publicity Office of the High Commissioner for New Zealand, London.

2. Non-Federated Spas and Health Resorts.

The places mentioned in the following list, while they do not comply in every respect with the requirements of the Federation, are all places of some importance, having either waters of distinct medicinal value or well-equipped medical baths —

BUILTH Saline, sulphur, and chalybeate springs
CHURCH STRETTON Climatic 'after-cure' resort
ILKLEY Climatic resort, several springs
LLANWRTYD Two mineral springs
MALVERN 'After cure' resort, very pure water
MATLOCK Hydropathic establishments
MOFFAT Waters and baths
NANTWICH Brine baths
NORTHWICH Brine baths
RIPON Saline waters and baths
SALTBURN Brine baths
SCARBOROUGH Mineral springs, baths and treatments
TORQUAY Climatic resort, seaweed baths and other treatments
TUNBRIDGE WELLS Saline chalybeate water, spa treatments

It should be added that medical baths and treatments are now obtainable at most of the leading seaside resorts, even where no natural mineral springs exist

BUILTH WELLS, Breconshire, picturesquely situated on the River Wye, 180 miles from London, has a mild climate There are two wells the Glanne Wells (sulphur and chalybeate) and the Park Wells (saline) Both are a short distance from the town

CHURCH STRETTON, Shropshire. Situated 160 miles from London in a valley at an elevation of about 700 feet above sea level, Church Stretton is sheltered on both east and west by wooded hills, and has a dry, bracing climate It is recommended as an 'after-cure' resort The water from the Cwm spring is noted for its purity

ILKLEY, Yorkshire. Situated on the River Wharfe, 210 miles from London and 16 from Leeds, Ilkley has very pure and stimulating air Several springs yield slightly mineralized waters As a resort, Ilkley is specially suitable for delicate children, for pulmonary tuberculosis, and for convalescence

LLANWRTYD WELLS, Breconshire. Situated at an elevation of 800 feet, 220 miles from London, Llanwrtyd is well sheltered by the high surrounding hills The Dolycoed Spring yields a pure sulphur water, the Victoria Springs contain also lithia and barium

MALVERN, Worcestershire. Malvern is the name given to a group of townships situated on the lower slopes of the Malvern Hills at an elevation of 500-800 feet. Great Malvern station is 122 miles (2½ hours) from Paddington.

Climate.—Dry, bracing, and equable. The air is very pure, and the winters are mild. As a climatic health resort Malvern is unique: easy hill-paths afford every degree of regulated exercise, while the pure dry air reduces fatigue to a minimum. Malvern is particularly suitable for cardiac cases. The district is rich in interest, and the views from various points on the hillside are extensive and beautiful.

Water.—The springs at St Ann's Well and Holy Well supply a water of remarkable purity, with scarcely any saline constituents. The water is available at the Pump Room in the Winter Garden.

Season.—Easter to late autumn. Music is given in the Priory Park; bathing and boating are available at the lake. Adjoining the Winter Garden is a theatre, where the Annual Dramatic Festival will be held this year from July 27 for four weeks.

Address.—The Spa Director, Rose Bank, Malvern, will answer inquiries and furnish illustrated guide and accommodation list free of charge.

MATLOCK, Derbyshire. Matlock is 144 miles from London and is easily reached by rail (L.M S.). It is beautifully situated on the slope of the hills overlooking the valley of the Derwent. The climate is equable and free from extremes. Mean temperature in winter 45°; average rainfall 32·21 inches. The situation is well sheltered, the outlook from any part is magnificent, and the southern exposure ensures a maximum of sunshine. The water supply, which comes from the open moorlands, is remarkable for its purity and softness, and the air, thanks to the drainage of moisture from the hillside, is dry and bracing.

Matlock is noted as a centre of hydrotherapy, the oldest and most famous of its hydros being Smedley's, which is situated about half-way up the hill, some 250 feet above the valley and about 500 feet above sea-level, in extensive grounds commanding a fine view. All forms of spa treatment are available at this hydro, which is open all the year round and maintains a large staff of trained attendants.

Matlock Bath is in the valley, about a mile south of Matlock. It has a small saline spring, and its climate is mild. Many places of interest are within easy reach, including Dovedale, Haddon Hall, and Chatsworth House.

MOFFAT, Dumfriesshire. One of the most accessible of the Scottish health resorts, about 340 miles (7½ hours) from London, and 60 miles (2 hours) from Edinburgh or Glasgow, on the L M S Railway, Moffat stands about 350 feet above sea-level in a picturesque pastoral district sheltered by hills and abounding in fine walks and drives The climate is bracing but not severe Season, April to October Moffat well water contains sulphur and salines, and is taken internally or used as baths The Baths are situated in the town, the Pump Room is a short distance from the town A chalybeate well at Hartfell is about five miles away, and is reached by a hill-path

Address—The Town Clerk, Moffat

NANTWICH and NORTHWICH, Cheshire. These towns, situated on the River Weaver, are respectively 160 and 170 miles from London Both places have brine baths, in which is used a brine containing about 20 to 25 per cent of total salts The baths at Northwich are controlled by the Corporation, those at Nantwich are in the Brine Baths Hotel building The brine is similar to that of Droitwich and is used for the same purposes

RIPON, Yorkshire Situated 212 miles from London, and a similar distance from Edinburgh, Ripon stands on a slight eminence and in open country It is about 11 miles by road from Harrogate The air is pure and invigorating and the climate mild and salubrious Ripon has interesting historical associations The Spa buildings are under Municipal control, and the water contains sulphur, strontium, and the usual saline ingredients

The Town Clerk will furnish guide-books and information free.

SALTBURN-BY-THE-SEA, Yorkshire. Pleasantly situated on the east coast to the north of Whitby, Saltburn is a popular seaside resort The town specializes in brine baths The brine, which is about the strength of that of Northwich is brought from brine wells twelve miles distant, and is used for various medical treatments

SCARBOROUGH, Yorkshire Scarborough is 230 miles (5 hours by rail) from London, and about the same distance from Edinburgh It is picturesquely situated on the east coast of Yorkshire on a rocky slope, facing the sun It has excellent sands and every facility for sea-bathing in safety The climate is mild in winter

Mineral Waters—The two saline chalybeate springs, which were discovered in 1620, are tonic and aperient, the two waters being very similar The Pump Room is situated on the Spa promenade

Treatments—The Corporation Medical Bath Establishment is centrally situated, and is equipped for the administration of electro-

therapeutic and hydropathic treatments, including medicated, russian, turkish, and seaweed solution baths, also various douche treatments. A large sunshine lounge is open to the public.

Season.—All the year round. Attractions include the Spa orchestra, beautifully laid out Cliff Gardens, spacious sands and promenades, beach bathing pool equipped with modern filtration and chlorination plant, facilities for sport, and various entertainments.

TORQUAY, South Devonshire. Torquay is 200 miles from Paddington and is served by express trains in 3½ hours. Rail services are available also from northern centres.

Climate.—One of the most beautifully situated health resorts in the British Isles, Torquay has a delightful climate, mild in winter and not too hot in summer, which makes it available all the year round. Humidity is low. Average figures for the past 35 years are: mean temperature 51·7°; rainfall 34·05 inches; sunshine 1766 hours; ultraviolet radiation (5 years' average) 3·36 units daily. The prevailing winds are westerly and south-westerly.

Treatments.—The Marine Spa, a well-appointed establishment owned by the Corporation, is equipped with the latest apparatus for hydrological, electrical, and accessory treatments, having been completely reconditioned during the last two years. Attendants are fully qualified, and a consulting-room is available for physicians. The establishment includes a vita-glass sun lounge, recently much enlarged and improved, and a large warm sea-water swimming bath.

Mineral Water.—The Corporation owns a spring, the water of which is hypotonic, and contains magnesium, calcium, and bicarbonate ions. It is recommended in bladder and urinary conditions, gastro-intestinal disorders, rheumatism, gout, and metabolic disturbances.

Address.—H. Berkeley Hollyer, General Manager, The Marine Spa, Torquay. A beautifully illustrated handbook will be sent free.

TUNBRIDGE WELLS, Kent. Royal Tunbridge Wells is delightfully situated on the Kent and Sussex border, within one hour from London. The climate is exhilarating and mildly bracing. Tunbridge Wells holds a high record for sunshine.

Waters.—The Wells are situated on the old-world Pantiles, the unique walk immortalized in the writings of Macaulay, Pepys, and others. The waters, which have been in use for over 300 years, are saline chalybeate. The usual spa treatments are available at the Sherwood Park Clinic, and at the Tunbridge Wells Hydro and Clinic, Mount Ephraim. Another spring, having a low mineral content but very rich in CO_2, has recently been discovered.

Address.—Spa Department, Town Hall.

3. The Spas of Ireland.

With its mild climate, its beautiful scenery, and the charming civility and proverbial good humour of its inhabitants, Ireland ought to be an ideal country for those seeking restoration of health No fewer than eight places in Ireland have mineral springs, and coast resorts are numerous Unfortunately, little has been done to develop the mineral springs of Ireland, and many of the places offering such treatment are obscure

BALLYNAHINCH, Co Down, 17 miles by rail from Belfast Waters sulphurous and chalybeate

BALLYSPELLAN, Co. Kilkenny; near Johnstown, little known outside its own county Water light chalybeate, with carbonic acid

CASTLECONNELL, Co Limerick, on the River Shannon about 6 miles from Limerick Waters mildly chalybeate

LISDOONVARNA, Co Clare, 7 miles from Ennistymon, the nearest railway station, where vehicles from the hotels meet all trains Climate healthy, scenery fine Several mineral springs, including sulphur, magnesia, and chalybeate waters all the waters contain iodine The new baths are now open, where the usual spa treatments may be had Address John Tierney, Secretary

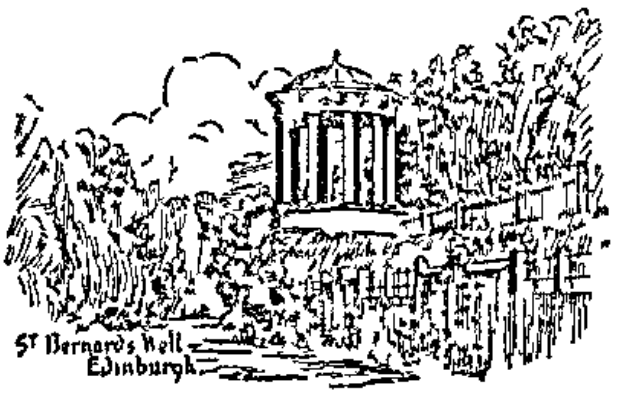
LUCAN, Co. Dublin, 8 miles from Dublin by electric tramway, frequented by visitors from the capital Water sulphurous

MALLOW, Co Cork. At one time Mallow Spa was one of the most frequented in Ireland There are several springs, chalybeate and thermal

SWANLINBAR, Co Cavan Another Irish spa once much frequented and now almost neglected Water sulphurous

TRALEE, Co Kerry Prettily situated on the north shore of the bay Water chalybeate

A full description of the Irish Health Resorts is given in a book bearing that title by D L Flinn, published by Fannin & Co, Dublin



REVIEWS OF BOOKS.

The United States Pharmacopoeia.

Just ten years after the issue of the tenth revision (1926) comes the Eleventh Decennial Revision of the Pharmacopoeia of the United States, which becomes official on 1st June of the present year. It appears four years after the British Pharmacopoeia of 1932, and in some respects it may be described as a revised edition of the British work. A glance at the new items shows that quite a number of these are already in our own volume, while others have come into being or into recognition since. Among the novelties one notices calcium gluconate, green iron and ammonium citrates, histamine phosphate, a liver extract for parenteral use, merbaphen, chiniofon (equivalent of 'yatren'), theophylline with ethylene diamine (aminophylline), and tryparsamide, none of which is as yet included in the British work.

The deletions are again very numerous and include such old favourites as saccharated carbonate of iron, compound powder of rhubarb (Gregory's powder), and sulphonal. A number of names have been changed, some only slightly so, as amidopyrine, which becomes aminopyrine, or balsam of Peru, which is now peruvian balsam. Among the more complete changes may be cited oil of cade, which becomes juniper tar (pix juniperi); pulvis glycyrrhizae compositus is now pulvis sennae compositus, while gluside has changed back to saccharin. Another change, and by no means a pleasant one, is the alteration of sulphur and sulphate to sulfur and sulfate. Fortunately this applies only to derivatives of sulphur: phenol still retains the 'ph,' for even America shies at 'fenol.'

A feature of the monographs is the introduction of graphic chemical formulae, which sometimes occupy an unnecessary amount of space. When the expression 'per cent.' is used without qualification in prescriptions for solutions it is to be interpreted as weight of solid in volume of liquid. A gratifying feature of this revision is the acknowledged co-operation of the British Pharmacopoeia Commission. Free exchange of reports and discussions has accompanied an effort to harmonize titles and standards as far as possible. The alternate appearance every five years of the British and American works should do much to ensure an international harmony which in these days is much to be desired. T. S.

A Text-book of Midwifery. By R. W. Johnstone, *C.B.E.*, M.D., etc., Professor of Midwifery, University of Edinburgh. Eighth Edition. Pp. 471. (A. & C. Black. 18s.)

The eighth edition of this excellent work has appeared little more than a year after the seventh. Very thorough revision is evident throughout the work. The section on antenatal care and hygiene has been largely rewritten and generally the work has been brought up to date in every respect. This work, which is one of the Edinburgh Medical Series, has by now achieved the position of a standard textbook. The author's style is lucid and pleasing and the book is admirably suited for both students and practitioners.

It is proposed to publish an ADDENDUM to the British Pharmacopoeia some time during the present year It will probably contain monographs on ascorbic acid, calciferol, a solution of calciferol in a vegetable oil to replace the present solution of irradiated ergosterol, and an adsorbate of vitamin B_2 Certain new assay processes are suggested and the doses of the Pharmacopoeia have been reviewed Among the new drugs to be included are ergometrine, calcium gluconate, and mersalyl The new United States Pharmacopoeia is being carefully studied with a view to adjustments in the direction of uniformity between the two works

MASSAGE AS A PROFESSION FOR THE BLIND is the subject of a Bulletin (No 10) published at sixpence by the National Institute for the Blind Massage, it is pointed out is pre eminently a profession by which those deprived of sight can gain not only independence but also a satisfactory knowledge that they are contributing to the welfare of their fellowmen The Institute is doing good work and is deserving of support

SCHOOL EDUCATION IN HYGIENE AND SEX is the title of a series of lectures given at Felsted School by G O Barber, M B B Ch , the medical officer of that school (Heffer, 2s 6d) Seven lectures, beginning with the digestive system and ending with venereal disease, are preceded by several forewords, including one by the Headmaster of the school. The author's approach in all the lectures is frank and elementary and admirably suited for boys it is an attempt to dispel ignorance In his treatment of fear, for example, he states that fear is inborn and is nothing to be ashamed of it is only by the development of our higher reasoning powers that we can decide what we ought to fear and what we ought not to fear An excellent little book for parents and teachers

Dr David Rorie whose book of verses ' The Auld Doctor ' we reviewed some years ago, has published an enlarged book of verse under the title of THE LUM HAT WANTIN' THE CROON the most popular of his works The verses are in ' braid Scots ' of the northern type, perhaps too phonetic in their spelling for easy reading although the glossary at the end is helpful The verses are clever, some of them reaching a high level, and will give special pleasure to medical readers who hail from north of the Border The book is published by the Moray Press 126 Princes Street, Edinburgh, at five shillings net

WHO'S WHO " 1936 (A & C Black 60s) the eighty eighth annual issue of this well known work has all the fascination of its predecessors With its 40,000 biographies in nearly 4000 pages it is a mine of information and one can open it anywhere and read with pleasure and profit Invaluable as a book of reference it is becoming more and more indispensable to anyone engaged in public work Its intrinsic interest is bringing it more and more into private houses, and it is by no means out of place in the physician s consulting room A copy of the current year's volume together with the companion volumes of ' Who Was Who,' provides an up to date biography of the nation and serves as a supplement to the ' Dictionary of National Biography '

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PROGRESS IN MEDICAL RESEARCH

EACH year about this time sees the appearance of the Annual Report of the Medical Research Council, which summarizes the work done during the past year.[1] While most of it has already been mentioned in these pages, it is interesting to review the year's work as a whole and as it is presented in the Report now before us.

Great emphasis is placed this year on the application of modern knowledge to the problems of nutrition. The importance of proper feeding in the maintenance of health has aroused the interest of the public, who now show an inclination to discuss the menu in terms of calories and vitamins. It is in the domain of vitamins that greatest progress has been made. Several of these food factors have been isolated: one at least has been synthesized, and international standards have been established on a chemical basis—the only really reliable basis for standardization. The relation of nutrition to anaemia and to goitre has been further studied, with the result that valuable contributions have been made towards the prevention of these diseases.

Another subject dealt with at some length in the Report relates to the alkaloids of ergot. The new water-soluble alkaloid ergometrine, isolated early in 1935, is said to be the principle responsible for its effect on the uterus in childbirth. According to the Report, ergot has at last given up its secret, and the practising physician can now administer pure ergometrine to his patients.

1. Report of the Medical Research Council for the Year 1934-1935. Pp. 183. London: H.M. Stationery Office 3s. net.

At last the principle to which liver owes its action in pernicious anaemia has been isolated—this was mentioned in our February issue. The substance has been prepared on a manufacturing scale in this country and has been tested clinically with most satisfactory results: injection of 0·1 to 0·2 gm. once weekly effected an increase in the red blood cells and in a few weeks the patients were restored to health. Its value in subacute combined degeneration of the spinal cord is being examined.

Puerperal sepsis is not only a cause of much maternal mortality but is also one of the great enigmas of medical science to-day. Recent work has shown it to be due to certain streptococci, carried chiefly in the nose and throat either of the patient herself or of her attendants. Now that this is understood it will be possible to exercise greater care to prevent such infection.

The work done on anaesthetics has been considerable: reference to it will be found in the succeeding pages of the present issue. Other subjects that have engaged the attention of the Council and its workers are standards for sex hormones and the relation of iodine to thyroid disease—these will be dealt with in our Endocrinology Number next month. Matters affecting industry—industrial pulmonary disease and the toxicity of industrial solvents—have been studied, as has also the relation of bed-bug infestation to public health. On all these questions the Report shows that considerable additions to knowledge have resulted.

The Report reviews the work done during the year ended September 30, 1935. The Council's work is subsidized by a grant-in-aid from the Treasury, which provides for the maintenance of the Institute at Hampstead and the Farm Laboratories at Mill Hill, and allows for grants to research workers. Scientific bodies interested in special subjects have augmented the Government grant to various extents, all of which contributions are duly acknowledged. The Council is also in constant touch with workers overseas whose interests are similar. The Report provides an interesting summary of the position of medical research at the moment.

ANAESTHESIA AND ANALGESIA:

A Year's Progress.

GENERAL ANAESTHESIA.

A REPORT recently issued by the Joint Anaesthetics Committee selected by the Medical Research Council and the Royal Society of Medicine covers eleven years' work The report is presented in considerable detail and deals with most of the anaesthetics at present in use Referring to the newer anaesthetic agents, the Committee reports that *ethylene* is now being manufactured in this country, but that its popularity has been restricted by its unpleasant smell and by the fear of explosions The first of these objections is being countered by the manufacture of a purer product *Vinyl ether* is favourably reported on, and is regarded as promising *Cyclopropane*, when it is available at a lower cost by being made in this country, is likely to prove of value, but as considerable skill is required in its use it will probably remain for the present in the hands of the specialist (HADFIELD)

Explosive Anaesthetics —A memorandum dealing with explosions of anaesthetics has been issued by the MINISTRY OF HEALTH The number of serious accidents due to this cause, says the memorandum, have so far been small, but two factors seem likely to increase the risk of such accidents—the administration of mixtures of ether and oxygen and the increasing use of electrical apparatus during anaesthesia Precautionary measures are therefore necessary and attention should be directed to the following points (1) A rich ether-oxygen mixture is more dangerous than a corresponding ether-air mixture and a very small spark suffices to cause ignition (2) Although nitrous oxide is not itself inflammable, it increases the inflammability of mixtures of ether with air or oxygen (3) Ethyl chloride yields a vapour which is explosive when mixed with air (4) A C E mixture may yield an explosive mixture with air (5) Ethylene-oxygen mixture is very destructively explosive Full details are given regarding the dangers to be guarded against and the precautions to be taken, such as ventilation, use of suitable anaesthetic apparatus, and protection from electric sparks and static electricity

Special Conditions —The question whether general inhalation anaesthesia is contraindicated in patients complicated by allergic conditions, especially those involving the respiratory passages, is the subject of a report by ANDRÉ and GROVE (New York) They conclude that general anaesthesia is as safe in allergic patients, even the severely asthmatic, as in other patients, provided (*a*) the cases are properly selected and prepared, (*b*) an operative method is used which combines light anaesthesia and carbon dioxide and

oxygen ventilation with a minimum risk of pulmonary complications, (c) careful postoperative treatment is carried out with the assistance of an allergist physician They describe a method of technique which fulfils the requirements laid down and they report that in a series of 204 cases of tonsillectomy and radical antrum operations pulmonary complications were entirely absent

Anaesthesia for thyrocardiac patients is dealt with by SISE (Boston), who defines such patients as those having thyroid toxicity and significant heart disease, including coronary disease, angina, mitral stenosis, and aortic regurgitation In such cases the gases are superior to local analgesia because the patients are usually nervous, the analgesia is inadequate, and the surgeon is restricted Of the gases, nitrous oxide is dangerous on account of anoxaemia The best anaesthetics are ethylene, cyclopropane, ethylene-cyclopropane, and ethylene ether Proper conduct of the anaesthesia is more important than the choice between these

Labour.—Dealing with relief of pain in labour, STACEY (Sheffield) mentions the use of anaesthetics in contradistinction to analgesics and says that he considers chloroform safe for use as a routine method He uses gas and oxygen, and also ether, in selected cases, where, for example, an element of shock is present, but he thinks that if a vote were taken of the anaesthetics used in labour chloroform would still head the list

A report by the BRITISH COLLEGE OF OBSTETRICIANS deals with the subject of analgesics suitable for administration by midwives The report states that gas and air administered by the Minnit apparatus (described in THE PRESCRIBER, April 1935, p 115) is a safe and satisfactory method of producing analgesia, although it is expensive In the absence of a definite contraindication it may be used by midwives and in hospitals having no resident medical officer Chloroform by any method should not be used by midwives acting alone Registered medical practitioners, aware of its dangers, can take precautions to lessen the risks Paraldehyde per rectum cannot be recommended for use by midwives, mainly because it does not provide adequate analgesia at the time of actual birth

Collapse during Anaesthesia —Complete recovery after cessation of cardiac action under anaesthesia is a rare occurrence, and such a case is reported by GRANT (Birkenhead) The operation (on the kidney) was done under percaine spinal analgesia supplemented by warm ether and oxygen During operation collapse set in, coramine failed to produce any reaction Artificial respiration was resorted to, and 5 c cm of adrenaline solution was injected into the heart but without result, probably because it went into the chamber of the left ventricle and not into the muscle After three minutes a second injection was given and within thirty seconds pulsation returned Breathing soon returned and the patient made a complete recovery with no sign of cerebral damage

GUILLEMAN (Paris) speaks highly of 'carbogen' as a remedy in cases of asphyxia and syncope during anaesthesia Carbogen is a mixture of carbon dioxide (7 per cent) and oxygen (93 per cent) and is given by inhalation in large doses It is a powerful stimulant of the bulbar centre and causes no ill effects, nervous symptoms or pulmonary complications never having been observed in its use

Blood-Pressure Changes —One of the chief anxieties of the anaesthetist is to maintain an efficient circulation during anaesthesia A gross fall in blood pressure is fraught with so much danger that it must be avoided at all costs It is pointed out by MAXWELL (Melbourne) that the moment the first surgical incision is made histamine, or a histamine like body (H substance), is liberated in the injured tissue, and this is very potent in inducing a fall of blood-pressure Fortunately, the tissue damage at the same time liberates adrenaline, which tends to antagonize the action of histamine This chemical mechanism produces a condition of physiological equilibrium, provided the damage to the tissues is not too extensive If, owing to preoperative injury, the tissues are greatly damaged, the liberation of histamine may be so overwhelming that the adrenaline output fails to check it, and symptoms of shock will follow In such cases the vasoconstrictor action of ephedrine is useful in combating a fall of blood pressure

Effect on the Heart —Electrocardiographic studies were made by KURTZ, BENNETT, and SHAPIRO (Madison, Wis) on 109 patients during surgical operations, the anaesthetics employed being cyclo propane (41), ether (20), procaine (13) ethylene (11), nitrous oxide (10), vinyl ether (7), chloroform (6) and avertin (5) Records were taken before operation, at frequent intervals during surgical procedure, during recovery, and ten hours after the operation Disturbances of rhythm were the most striking changes noted Arrhythmias appeared more frequently in abnormal than in normal hearts the lowest incidence occurred with procaine and the highest with chloroform Of the entire series only 21 per cent failed to show some type of disturbance No constant and specific relationship could be established between the occurrence of arrhythmias and the depth of anaesthesia or the steps in the surgical procedure

Premedication —In stressing the value and importance of premedication, MIDDLETON (Edinburgh) mentions certain necessary precautions In certain operations premedication should be minimal For operations on the mouth, pharynx, and upper air passages, any measure which retards complete recovery of consciousness, and in particular the return of the laryngeal reflex, is undesirable and increases the risk of an aspiration pneumonia It is probable that in operations such as pulmonary lobectomy any depressant of the respiratory centre should be avoided When preoperative sedation or narcosis is employed, the anaesthetist should be responsible for the choice of drug and the method of its use

Basal Narcosis—The employment of basal narcosis (a term preferable to 'basal anaesthesia') is now much in favour It is more than merely a preliminary to general anaesthesia, being an actual part of the anaesthetizing process Given by rectum (avertin or paraldehyde) or intravenously, or even orally in some cases (barbiturates), while the patient is still in bed, it induces a narcosis which not only protects the patient from psychic shock but admits of the use of a much smaller quantity of the general anaesthetic, while the subsequent somnolence, which lasts for some time, diminishes after-pain and liability to vomiting Its disadvantages are the difficulty of adjusting the correct dosage, the necessity for more careful nursing after operation, and occasional restlessness

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AVERTIN.

The properties of avertin (tribromethyl alcohol or tribromethanol) and the technique of its administration are now well known It is a white powder and is given by rectum in aqueous solution The dose is 0 08 to 0 1 gm per kg of body-weight (5¼ to 6¾ grains per 10 lb), the required quantity being dissolved in water to make a 3 per cent solution The temperature of this solution must be maintained carefully at 35°-40° C (95°-104° F) and must on no account exceed the higher figure, as decomposition readily occurs, yielding acid products extremely irritating to the intestine Freedom from acidity is indicated by addition of a few drops of congo red solution 'Fluid avertin,' a solution in amylene hydrate containing 1 gm in 1 c cm, is issued for convenience in preparing the solution

In a general review of the subject, SHIPWAY (London) gives an analysis of 1600 administrations of avertin, from which he draws the following conclusions (1) The dosage should be individual

(2) Given in accordance with established principles avertin can be used with complete safety (3) Drugs which depress respiration should not be given before avertin until the anaesthetist has gained full experience of its action Larger doses of avertin are preferable in difficult subjects (4) Liver and kidney disease are not contra-indications to its use, but call for reasoned dosage, nitrous oxide with oxygen is preferable to ether (6) Avertin reduces postoperative morbidity and mortality

HOTTEN (Sydney) is inclined to be critical Avertin, he says, is a far more powerful drug than paraldehyde and extreme care is necessary in measuring the dose and preparing the solution, a matter the anaesthetist must personally attend to If the solution is run in very slowly the patient may fall asleep before the injection is completed Occasionally patients become restless or excitable during administration, but this is unusual The airway must be carefully watched lest the relaxation of the muscles obstructs respiration Should cyanosis become marked without such obstruction, the following measures must be adopted without delay (1) injection of coramine, (2) administration of 5 to 10 per cent carbon dioxide and oxygen, (3) high rectal irrigation with warm hypertonic sodium thiosulphate, (4) ephedrine, ¾ to 1½ grain hypodermically. These drugs should always be at hand Chloroform is not advisable as a general anaesthetic after avertin In the postoperative period patients require watching for a long period lest the tongue should drop back Avertin narcosis with local infiltration analgesia is a very useful combination for intracranial surgery

Dealing with the influence of avertin upon the renal function, PITT (London) says that in spite of the conditions which tend to hamper the renal function during anaesthesia, nitrogen excretion is actually very little upset by the volatile anaesthetics and less so by avertin Even with the decreasing reserve of kidney function after middle age, it does not assume dangerous proportions, and of itself the influence of avertin upon the kidneys forms no contra-indication to its use in older patients

REYCRAFT (Cleveland, Ohio) records a critical study of 429 major gynaecological operations in which avertin was used He concludes that it is a safe basal narcotic in such cases if the known contra-indications and dangers are heeded A safe dose is not more than 0 07 gm per kg, serious complications may attend administration of larger doses Avertin may be combined with a barbiturate so long as there is no idiosyncrasy on the part of the patient Post-operative nausea and vomiting were absent in 60 to 75 per cent of the patients studied, indeed these effects were found to be in direct proportion to the concentration of ether subsequently used

HEARD (Toronto) reports its use in thyroid surgery, in which he regards it as of pre eminent value In sixty cases it was used as a basal narcotic followed by nitrous oxide and oxygen—not ether, which is unsafe in such cases It may be, Heard says, that local

analgesia will eventually be the method of choice in thyroid operations but assuming that a general anaesthetic is desired avertin followed by nitrous oxide is undoubtedly best

BOYD (Belfast) recommends its use as a complete anaesthetic for children From his experience of 700 cases he concludes that avertin can be given to children as a complete anaesthetic with safety provided a careful look out is kept for danger signals and the patient is treated accordingly It is much safer in children than in adults as there is better detoxication and elimination The best method of administration to produce complete anaesthesia is to combine avertin 0 175 gm per kg body weight with morphine and atropine according to age and 20 to 30 c cm of procaine as a field block The depth of anaesthesia is best assessed by nipping the skin of the neck and watching the arm for movements The fall in blood pressure is not of serious moment Complete avertin anaesthesia is contraindicated in very young and very cachectic children

ASHWORTH (Manchester) reports a case in which an unusually large dose of avertin was given The patient was a woman weighing about 25 stone (350 lb) in whom it was desirable to reduce the inhalation anaesthetic to a minimum She received 0 09 gm of avertin per kg of body weight the amount of fluid avertin administered being diluted to 558 c cm (about 19 fluid ounces) for rectal injection This was followed by ether anaesthesia The operation was performed successfully and the patient made an uninterrupted and complete recovery

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BARBITURATES

The use of the derivatives of barbituric acid (malonyl urea) as basal narcotics has of late made rapid progress The barbiturates at present recommended for this purpose are dial evipan hebaral sodium nembutal sodium amytal pentothal pernocton rectidon and eunarcon These are dealt with in order in the succeeding pages

The employment of barbiturates in primiparous labours is reported by TRITSCH and BROWN (New York) who tried various

products, such as dial sodium amytal, and sodium alurate, in combination with morphine, omnopon, scopolamine, and rectal ether It is concluded that for relief of pain and production of amnesia in labour the barbiturates act better and for a longer time when combined with other drugs Rectal ether appears to delay labour, while labour was shortest when the greatest degree of analgesia and amnesia was obtained Excitement was observed in about 25 per cent of the cases, this was aggravated by scopolamine and lessened by omnopon and by morphine Apnoea in the infants was frequent and was aggravated by omnopon

Discussing the use of barbiturates in obstetric analgesia, KICKHAM and TITUS (Boston) remark on the great increase in the use of these during the past five years The drugs most commonly used are sodium-amytal and nembutal, the latter being now very popular Excitement and restlessness are rarer with nembutal than with amytal Barbiturates should not be given to cardiac patients, or soon after eating Drop ether is preferable to gas oxygen as a terminal anaesthetic, as many patients take the latter very badly

Dial—This 'ciba' compound is diallylbarbituric acid and its equivalent is allobarbitone B P C A preparation which has given good results in obstetric practice is dial urethane a combination of dial and urethane, the latter rendering the compound water soluble Dial itself has also been used for relief of labour pains

Evipan.—This 'Bayer' product known in America as evipal, is of recent introduction (1932) and is still the subject of numerous reports Chemically it is N methyl cyclohexenyl methyl barbituric acid, and it occurs as a white powder scarcely soluble in water The sodium salt, evipan sodium, is freely soluble and is employed as an intravenous general anaesthetic Evipan itself is used as a hypnotic The outstanding characters of evipan and its sodium salt are the rapid onset, depth, and short duration of narcosis, and the wide margin between the anaesthetic and the lethal dose

For use as a hypnotic evipan is supplied in tablets of 0 25 gm (4 grains), the dose being 4 to 8 grains or more For anaesthetic purposes evipan sodium is administered intravenously as a 10 per cent solution While it is freely soluble in water, the solution is very unstable and must be freshly prepared just before use For this reason the salt is supplied dry in ampoules having a capacity of 10 c cm and containing one gramme of the powder, each ampoule is accompanied by another containing 10 5 c cm of sterile distilled water This water is transferred by means of a syringe to the ampoule containing the salt, and a 10 per cent solution is thus readily prepared

The Anaesthetics Committee of the Medical Research Council reported on evipan in 1933, the following being a brief recapitulation of the conclusions of the Committee evipan sodium is not to be regarded as a basal narcotic, its action being too evanescent It

induces rapid, deep, and transient anaesthesia for short operations lasting not more than twenty minutes Restlessness is rare, unconsciousness is rapid and pleasant, recovery is free from unpleasant after effects Twitching of the facial muscles is frequent, and sometimes jactitation of the limbs occurs Since that report was issued, nearly three years ago, numerous independent observers have *recorded their experience*

JARMAN and ABEL (London), whose previous reports have been quoted in recent reviews (PRESCRIBER, 1934, Apr, 117, 1935, Apr, 113), have issued a further report They have used evipan-sodium in over 2000 cases as a basal narcotic or as a general anaesthetic, the cases being (*a*) minor operations on out-patients and (*b*) operations on in-patients In out-patients anaesthesia is usually required for only a few moments, and premedication is unnecessary The minimum dose is given, usually 2 5 to 3 0 c cm of the 10 per cent solution intravenously The *patient is awake in two or three minutes* and is able to go home after twenty to thirty minutes The first 2 5 or 3 c cm is injected fairly quickly (in five to ten seconds), and then a pause of thirty seconds is made to allow for the complete circulation of the blood If consciousness is not lost then, a further 2 to 3 c cm is injected For operations on in-patients premedication is given, preferably omnopon scopolamine, one hour before the evipan sodium, which is given as above at the rate of one c cm every two or three seconds For minor operations the full dose of 10 c cm is given In major operations this dose may be repeated as often as required during the operation, four injections can be given over a period of two hours Evipan sodium may be supplemented by gas oxygen or by spinal analgesia ether is not advised A free airway must be maintained and evipan sodium should never be administered *single-handed* *Coramine is best for collapse, and* for respiratory failure alpha lobeline intravenously or insufflation with carbon dioxide (7½ per cent) in oxygen

DOUGLAS discusses the use of evipan sodium in general practice He does not agree with Jarman and Abel that it should never be given single handed, as in his experience sagging of the jaw is infrequent, at least with small or moderate doses For two years he has used evipan sodium in all types of cases which a general practitioner is likely to meet in the everyday round, and he carries the necessary appliances in his 'little black bag' While evipan-sodium can safely be injected on a full stomach, he prefers when time permits to feed patients on tinned fruit and glucose before operation He has noticed that in many patients, as soon as injection is completed, the arms become stiff, flexed at the elbows and wrists, with the fingers extended and the thumb adducted across the palm

WRIGHT (London) remarks that anaesthesia with evipan sodium is often marred by faulty intravenous technique Numerous punctures may be made because the vein is not readily found or because the needle slips out He gives full details of a technique

which, if followed, will make for smooth working The patient's arm is fixed on an aluminium splint, with a pneumatic armlet to dilate the veins, the syringe and needle are fixed in place with strips of adhesive plaster, and a special mouth prop is used to maintain the airway For full details of this technique the original should be consulted

NICHOL (London) has found in 120 cases that premedication with omnopon ($\frac{1}{3}$ grain) and hyoscine hydrobromide ($\frac{1}{150}$ grain) greatly facilitates the action of evipan sodium He adds that such premedication has no definite contraindications, that a clue to the successful use of evipan-sodium is a very careful observation of the patient's respiration, and that to guard against any respiratory depression a sufficiently long interval must elapse between the preliminary medication and the injection of evipan sodium—one hour is the minimum and an hour and a half the optimum period

The use of evipan sodium in ophthalmic surgery was mentioned in last year's review (PRESCRIBER, 1935, Apr, 115), where it was stated that LYLE and FENTON (Westminster Ophth Hosp) had used it in 86 cases without premedication and with most satisfactory results In a more recent communication these workers report its use in over 200 cases and state that subsequent experience fully confirms their high opinion of it They now use omnopon and scopolamine as premedication and find that the amount of evipan-sodium required is materially reduced In patients anaesthetized with evipan-sodium a violent sneezing sometimes occurs on manipulation of the conjunctiva this may cause trouble if a knife happens to be in the eyeball at the time Cocainization of the conjunctiva before operation usually abolishes this reflex The fall of intraocular tension when this is raised, as in glaucoma, is an added advantage of evipan anaesthesia for operative purposes it may even be employed as a therapeutic measure, the reduced tension allowing the eye to respond to eserine, so that operation may be postponed to a more propitious moment

JOHNSTONE (Wolverhampton) is less enthusiastic, enlarging on its disadvantages While fully admitting the good qualities of evipan sodium in certain respects, he points out first that undesirable reflexes such as sneezing, coughing, or muscular twitching cannot be passed over lightly Sneezing inevitably sends up the intraocular tension to the limit of safety or even beyond it Muscular twitchings may send the needle out of the vein or hinder operative work He records two cases of severe postoperative nausea, while other complications (insomnia, headache, cardiac weakness) have been encountered He concludes with the observation that the ophthalmic cases requiring a general anaesthetic are few, and that careful retrobulbar anaesthesia diminishes the number still more

Reports from abroad come from many parts of the world BANERJEE (Calcutta) has used it with satisfaction in seventy-eight minor operations, his experience generally confirming that of

observers in this country PRASAD and SEN (Patna) report animal experiments to show that it raises blood pressure in anaesthetic doses HOLMAN and MATHIEU (Portland, Oregon) report 100 gynaecological operations done under evipan-sodium anaesthesia with completely satisfactory results GREENBERGER and BASS (New York) report fifty two urological cases in which evipan sodium was used They recommend it for cystotomy, prostatectomy, and orchidectomy, but the tremors produced render it unsuitable for use in cystoscopy, in which caudal analgesia is preferable MERRITT (Fall River, Mass) also finds it useful in urology WOO (Hongkong) reports its use in 100 cases including both major and minor operations His results appear to have been good WANG (Tongshan) also speaks highly of its use in minor operations Reports from the continent of Europe, chiefly from Germany, are particularly numerous, but they convey little that has not already been mentioned

Hebaral-Sodium —This is the sodium salt of hexyl ethyl barbituric acid, it is known in America as *Ortal sodium* (Parke, Davis) It is speedy in action and of low toxicity, and it is rapidly eliminated without unpleasant after effects It is supplied in 3 grain capsules, the dose being 3 to 6 grains As a basal narcotic, 3 grains will induce mild hypnosis if given four hours prior to operation, 6 grains will have the same effect if given one hour before operation

Nembutal (Pentobarbital-Sodium) —This is the monosodium salt of ethyl (1 methylbutyl) barbituric acid, it differs from soluble barbitone, B P, which is sodium diethylbarbiturate, in that one of the ethyl groups is replaced by a methyl butyl group Nembutal is a white powder, very soluble in water, forming an alkaline solution Aqueous solutions decompose on standing, on boiling a precipitation occurs with liberation of ammonia Nembutal may be given orally, by rectum, or intravenously, but the intravenous route should be employed only in cases where other methods are not feasible The dose as a hypnotic is 0 1 gm (1½ grain) orally, as a basal narcotic 0 2 gm (3 grains), for infants it may be given rectally as enema or as suppository in the following doses under one year ½ grain, one to three years 1 grain, for adults the rectal dose is 5 to 6 grains Nembutal is a product of the Abbott Laboratories

BURKWALL (Hainan, China) has given nembutal in obstetrical practice by intramuscular injection, which he found could be done into the gluteal muscles without any local reaction So given in doses of 3, 4, and 5 grains it produced satisfactory analgesia in a number of cases Two patients became excited and two slightly cyanotic, but these conditions were soon brought under control Later he used it intravenously in minor surgical cases, also as a basal narcotic and as a preliminary to evipan In all cases the pulse and respiration remained very little changed, but the blood pressure fell some 10 15 mm The drug was given also in some medical cases—psychoses, brain abscess, and tetanus—in doses of 5 grains

orally, intramuscularly, and intravenously, and in most cases gave very good sedative results Burkwall concludes that nembutal is of distinct value as a basal narcotic and for obstetric analgesia, while its use as the sole anaesthetic in surgery is limited to employment by skilled and experienced anaesthetists

HOTTEN (Sydney) expresses preference for nembutal as a basal narcotic for several reasons smaller doses give the desired result, being unstable it is more rapidly detoxicated, and therefore its hypnotic action is of shorter duration, there is less tendency to postanaesthetic restlessness As a preliminary to ether anaesthesia he gives 1½ grain the night before and 3 grains in the morning an hour and a half before operation though the morning dose is subject to modification Some patients appear to wake up on removal to the theatre, but they are so drowsy that they have no recollection of it afterwards Induction is started with ethyl chloride and this is followed by ether, of which less is required than without premedication Postanaesthetic vomiting is reduced When nitrous oxide is used, he gives ⅙ grain of morphine in addition to nembutal For children he gives a suppository of ½ to ¾ grain according to age

RAWLINGS (New South Wales) finds that nembutal, given orally as an analgesic and amnesic, is a useful adjunct in obstetric work It is best administered in small doses as required, patients react differently and he does not advocate large doses The time to commence administration is when the patient is in regular labour The case is reviewed hourly for further administration In prolonged administration watch must be kept on the respirations The drug does not tend to delay the second or third stages of labour, except in a few cases where the patient is very drowsy In the usual dosage it does not affect mother or child

BOYLAN (New York) reports its use as an obstetric analgesic in 205 cases, with no maternal mortality and no foetal mortality that could be attributed to the drug Labour was not inhibited and the delivery anaesthetic was reduced Excitement occurred infrequently and was controllable Combined with scopolamine it was even more effective

ROSS (Washington) treated thirty five cases of pre eclampsia with nembutal and found that it prevented the onset of convulsions, whereas three patients treated without nembutal developed convulsions In twenty-four cases of eclampsia the drug promptly stopped and completely controlled the convulsions With the control of convulsions the toxaemia subsided

JARMAN (London) reports on the use of nembutal in children In a large number of cases it has been most successful when given by mouth in doses ranging from ½ to 2 grains according to age, but sometimes it fails to act when so given, probably because the child has been eating shortly before or because its stomach is acid and this neutralizes the nembutal Jarman tried giving it in the form of suppositories, the dose being finally determined at one grain for

each year of age (excluding children of one year) up to 6 grains for 6 to 8 years After the age of 8 years the drug may be given orally These suppositories take from two to four hours to act and the suppository should therefore be given at least three hours before the operation Jarman has used nembutal in this way in nearly 200 cases without any unpleasant after effects being noted There never has been complete failure, as has happened with the oral route Nembutal suppositories (one grain) have been found to have a good effect in whooping cough in the few cases in which it has been tried it has given the child a perfect night's rest with complete relief from coughing

HORSLEY (Dorset Mental Hosp.) confirms Jarman's finding that the rectal administration of nembutal is never a complete failure as the oral method sometimes proves to be He has given it rectally in a number of mental cases the patient's individual response being first tested by a preliminary dose of 2 grains at bedtime, when most patients responded by sleeping for an average of six hours In certain manic states it was necessary to increase the dose to 6 grains which was found to be safe and usually effective Good results were obtained also in many cases of agitated melancholia and in the restless states of senile confusion

Pentothal-Sodium —Originally known as thiobarbiturate 8064 (Abbott) this compound is still in the experimental stage It is a yellow crystalline powder soluble in water Pentothal is administered intravenously like evipan and like it the solution must be prepared freshly as required JARMAN and ABEL (London) have tried this anaesthetic in over 1000 cases with no deaths and no unpleasant after effects except vomiting in a few cases that had had premedication Induction is smooth and the twitching or jactitation occasionally seen with other barbiturates is scarcely ever evident while the fall in blood pressure is less noticeable Its main disadvantage is that it is more depressant to the respiratory centre carbon dioxide and oxygen should be ready for use if required Pentothal is contra indicated in jaundice or hepatic disease and in low blood pressure Premedication is not desirable Jarman and Abel regard pentothal sodium as a worthy addition to the list of safe and satisfactory intravenous anaesthetics

Pernocton —This is the sodium salt of secondary butyl β bromallyl barbituric acid It is issued by Riedel in ampoules containing 2 c.cm. of a 10 per cent solution It is known in U.S.A. as 'pernoston' On the Continent it is popular as a basal narcotic and is usually given intravenously SIEPERT (Berlin) recommends its administration in tablet form by mouth So given it produces a deep sleep swiftly acquired and lasting from six to seven hours and having no disagreeable after effects Increase of dose is not necessary if used for some time on the contrary patients who begin with 0.4 gm. are usually able to reduce the dose to 0.2 gm. It should not be given to patients with heart disease

Rectidon.—This is described by the makers as a higher homologue of pernocton; it is administered rectally as a basal narcotic. Several reports have appeared of its use to produce amnesia in obstetrics. JONAS (Leipzig) has given it in fifty-three cases of labour. The drug was administered by rectal injection through a catheter three hours before delivery was expected. It takes effect in fifteen minutes. In ten cases complete analgesia was obtained; in seven it failed, and in the remainder a varying degree of analgesia resulted. In most cases of failure this was due to the drug escaping again from the rectum. In a few cases restlessness and excitement were observed.

Eunarcon.—This drug, formerly known as R. 1238, is a 10 per cent. solution of the water-soluble sodium salt of isopropyl-β-bromallyl-methyl-barbituric acid. It is put up in ampoules for intravenous injection, and is used mainly as a general anaesthetic. DÖRING (Berlin-Charlottenburg) has used it in 600 cases of general anaesthesia. The solution should be injected very slowly, and while the dose varies with different patients, 10 c.cm. should never be exceeded. If the pain reflexes are not abolished induction should be continued with ether. Prolonged anaesthesia, up to two hours, may be maintained by further injections in divided doses to a total of 20 c.cm. Respiration must be watched as cyanosis with respiratory failure may occur if the drug is injected too quickly. SCHRANK and DAHLHEIM (Berlin-Tempelhof) also report on its use for short narcosis.

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CYCLOPROPANE.

One of the most promising of recent additions to the list of general anaesthetics is cyclopropane, a gas said to be as innocuous as nitrous oxide, yet far more potent and giving better muscular relaxation Hitherto its cost has been high, all supplies coming from America, but more recently improvements in the process of manufacture have reduced its cost somewhat, and as it is now being made in this country it will most probably soon be available at a reasonable figure The question of cost is less serious than might be supposed, as very little is required to produce anaesthesia

Cyclopropane, or trimethylene, CH_2 CH_2 CH_2, is a cyclic isomer of propylene, CH_3 CH CH_2, and is related to ethylene, CH_2 CH_2. It is a colourless heavy gas (sp gr 1 46) with a sweetish odour, and is explosive in concentrations of less than 10 per cent. It does not irritate on inhalation and it is rapidly eliminated, allowing of rapid return to consciousness It is exceedingly soluble in lipoids; one part of olive oil dissolves more than one hundred parts of cyclopropane

The anaesthetic properties of cyclopropane were first reported from Canada in 1929, and a brief reference to this was made in our review of April 1930, p 138 Clinical reports did not begin to appear until two years ago, when the gas had become available commercially.

Reviewing its use as an anaesthetic, ROWBOTHAM (London) remarks that it has the potency of chloroform without its depressing effect on the circulation Its chief usefulness is for obtaining deep anaesthesia or for fortifying gas-and-oxygen Its real disadvantage is its tendency to cause capillary bleeding In one or two cases of high blood-pressure no ill-effects were observed Induction is pleasant, although the gas has an unpleasant odour, patients do not seem to notice it. Complete abdominal relaxation was obtained every time. Great care is necessary in its administration as it is neither a respiratory stimulant nor an irritant, but in the hands of the expert it is an anaesthetic of great utility and value. In another communication, ROWBOTHAM, CHESTER, JARMAN, PHILLIPS, and

VAILE report on its use in 250 cases during eighteen months, their conclusions being those given above.

Reports from America are more numerous. WOOD (New York) advocates the combined use of fluid avertin and cyclopropane. A cleansing enema is given the night before, then an hour and a half before operation a hypodermic injection of morphine sulphate $\frac{1}{8}$ grain and atropine sulphate $\frac{1}{150}$ grain. About 30-45 minutes before operation fluid avertin is given rectally in suitable dose, and anaesthesia is finally effected with cyclopropane. He finds that while avertin and cyclopropane by themselves depress the respiration, such depression is hardly ever observed when both are used together in this way. The combined method has given excellent results in over 750 cases.

SISE, WOODBRIDGE, and EVERSOLE (Boston) report 184 operations under cyclopropane, of which 124 were on the chest, and they think that the special value of this anaesthetic lies in its application to thoracic surgery. Its explosive nature must be borne in mind, and a carbon dioxide absorption technique is essential in its use. Cyclopropane is solvent for rubber, and the pin type of valve is most suitable, but in low concentrations rubber tubing, etc., may safely be used. Its great power and rapidity of action must be kept constantly in mind. At their clinic it has been found best to omit all premedication except morphine, $\frac{1}{8}$ grain, and scopolamine, $\frac{1}{100}$ to $\frac{1}{150}$ grain.

GRIFFITH (Montreal), whose previous work on this anaesthetic was mentioned last year (PRESCRIBER, 1935, Apr., 110), now records 1108 cases, in 90 per cent. of which he has obtained adequate relaxation without addition of ether. In the few abdominal cases in which an additional anaesthetic was required a very small amount of chloroform sufficed. In 371 cases he used avertin premedication, a combination which he regards as almost ideal. With a closed circuit the danger of explosion is relatively slight. With cyclopropane there is more tendency to capillary oozing than with ether.

ROVENSTINE (Madison, Wis.) commends cyclopropane in thoracic surgery because the respirations are not stimulated. Intratracheal operations are facilitated and the mucous membrane is not irritated, but the cautery cannot be used with safety.

ROMBERGER (La Fayette, Indiana) shows that on account of the rapid and powerful action of cyclopropane the various stages of anaesthesia are less easily recognised than with other anaesthetics. He describes three stages: (1) induction stage, in which the lid reflex is present; (2) moderate anaesthesia, characterized by oscillation of the eyeballs, which decreases with the depth of anaesthesia to the point of central fixation, this marking the entry of (3) deep anaesthesia, in which the depth of respiration is the guide, the deepest stage permissible being that at which the respiratory movements are just arrested, but the colour is pink and the pulse good. At this stage the depth of anaesthesia is readily reduced by increasing the percentage of oxygen and perhaps inflating the lungs a few times.

SCHMIDT and WATERS (Madison, Wis.) give a statistical comparison of the postoperative morbidity and mortality attendant on cyclopropane and other agents. Two groups of over 2000 cases each were treated under identical conditions, one group with cyclopropane and the other with ether, nitrous oxide, and ethylene. The figures for respiratory complications were definitely in favour of cyclopropane, but those for circulatory complications (haemorrhage, toxaemia) and for postoperative deaths were in favour of the other methods.

GRIFFITH, H R. Cyclopropane anesthesia *Anesth & Analg*, 1935, Nov.-Dec., 253.
ROMBERGER, F. T. Signs and phases of cyclopropane anesthesia *Anesth and Analg*, 1935, Mar.-Apr., 65-68
ROVENSTINE, L A. Cyclopropane anesthesia *Anesth & Analg*, 1935, Nov.-Dec., 270
ROWBOTHAM, S. Cyclopropane *Proc. Roy Soc Med*, 1936, Jan., 257-262
ROWBOTHAM, S, CHESTER, A, JARMAN, R, PHILLIPS, G R, and VAILE, T B. Cyclopropane anaesthesia a report based on 250 cases *Lancet*, 1935, Nov. 16, 1110-1113
SCHMIDT, E R, and WATERS, R M. Cyclopropane anesthesia: postoperative *morbidity in 2200 cases Anesth & Analg, 1935, Jan.-Feb., 1-3.*
SISE, L F., WOODBRIDGE, P D, and EVERSOLE, U H. Cyclopropane: a new and valuable gas anaesthetic *New England J Med*, 1935, Aug 15, 303-308
WOOD, P M. Clinical use of cyclopropane and tribromethanol in amylene hydrate. *J A.M A*, 1936, Jan 25, 275-279

ETHER.

The use of the ether-oil rectal method of inducing analgesia in obstetrics is dealt with by GWATHMEY and MCCORMICK (New York and Indianapolis), who describe an improved technique for its administration. A cleansing enema is first given, and two doses of nembutal (3 grains and 1½ grain) are given orally; with the second dose morphine (⅙ to ¼ grain) is given hypodermically. As the effects of the morphine begin to wear off, the ether-oil mixture is given by rectum and repeated as often as required: this consists of ether, 2½ ounces; quinine alkaloid, 20 grains; alcohol, 45 minims; paraldehyde, 120 minims; liquid paraffin or olive oil to make 4 ounces. This method, these workers say, is safe; it has no major physical contraindications and may be given to patients with cardiac disease, tuberculosis, etc. It gives satisfactory analgesia in 85 to 95 per cent. of cases, and most failures are due to faulty technique.

The subject of ether convulsions is still being discussed. A case is reported by WILLWAY (Manchester) in which a young girl developed convulsions under deep ether anaesthesia preceded by ethyl chloride. Ether was stopped, and under oxygen and carbon dioxide the patient recovered. Two days later a second operation was found to be necessary and ether on an open mask was used. No convulsions occurred. Toxaemia was present throughout both operations and was more severe in the second. In the first operation ether was pushed and anaesthesia was deep. Willway thinks that this case disproves the suggestion that an 'ether convulsion diathesis' exists.

ASHWORTH (Manchester) disputes this conclusion and holds that the precipitating factor was the deep anaesthesia. WRIGHT (London) agrees with Ashworth and adds two other factors which he thinks predispose to convulsions—preoperative atropine and the practice of covering the patient's body with rubber sheets, both of which tend to raise the patient's temperature. SMITH (Co. Cork) thinks that Willway's 'convulsions' were merely muscle spasms due to the ethyl chloride used as a preliminary, while CORFIELD (Bristol) adds that ether tremors of the lower limbs should never be confused with convulsions.

KING (New York) reports a fatal case in which a woman aged 38 under operation for gangrenous appendix developed convulsions as the peritoneum was being closed. Oxygen had no effect, but calcium gluconate intravenously gave some relief. The convulsions ultimately ceased, but coma supervened with pulmonary oedema and the patient died fifty-eight hours after the operation.

ASHWORTH, H. K Ether convulsions (corresp.) *B.M.J.*, 1935, Apr 20, 851.
CORFIELD, C. Ether convulsions (corresp.) *B.M.J.*, 1935, May 18, 1052.
GWATHMEY, J. T., and MCCORMICK, C O Ether-oil rectal analgesia in obstetrics: modified technic *J.A.M.A.*, 1935, Dec 21, 2044-2047
KING, H. J. Convulsions under ether anesthesia *Amer J Surgery*, 1935, Oct., 182-184
SMITH, P. J. Ether convulsions (corresp.) *B.M.J.*, 1935, Apr. 27, 901.
WILLWAY, F. W Ether convulsions with normal behaviour during subsequent ether anaesthesia *B.M.J.*, 1935, Apr. 13, 764.
WRIGHT, A. D Ether convulsions (corresp.) *B.M.J.*, 1935, May 4, 949.

NITROUS OXIDE.

According to MINNITT (Liverpool), the best analgesic for children, and the simplest to use, is nitrous oxide gas It has a very faint smell, a slightly sweet taste, and a sp. gr. of 1·527—it is heavier than air. If the gas is allowed to flow gently from a delivery tube it will sink through the air. When a patient inhales this gas mixed with air for a short time sleep supervenes. If, therefore, the child's attention can be directed towards something interesting, while the air breathed contains nitrous oxide gas in sufficient quantity, sleep will quietly develop without his knowledge. Minnitt has devised a mask, at the upper end of which are three painted disks—red, yellow, and green. This is held in front of the child's face, so that the coloured disks can be seen easily, and 100 per cent. gas is allowed to flow so slowly into the face-mask that the current is inappreciable. The child is asked to watch the red disk and to say when it changes colour. While he is waiting expectantly the analgesia develops. The eyelids droop and then close, until gradually unconsciousness is peacefully obtained. The mask can now be carefully lowered until it rests upon the face: analgesia becomes anaesthesia, and any anaesthetic may be continued as desired.

MINNITT, R. J. Gas-air analgesia as an aid to anaesthesia in children. *Liverpool Med.-Chir. J.*, 1935, part 2, 120-123.

PARALDEHYDE.

The use of paraldehyde as a basal narcotic is discussed by HOTTEN (Sydney). He has found it particularly useful in very nervous patients, in children, and in cases of thyrotoxicosis. It does not produce the same degree of narcosis as avertin, nor has it the same depressant effect on the circulation and respiration. On account of its unpleasant smell it is best given by rectum. The dose is 45 to 60 minims per 14 lb. body-weight, with a maximum dose of 1½ fluid ounce (40 c.cm.). The paraldehyde is mixed with olive oil, milk, or normal saline solution—this last facilitates absorption by the bowel: one part of paraldehyde is added to ten parts of saline solution and mixed by shaking. The paraldehyde must be pure and should be kept in a well-stoppered bottle as it readily oxidizes, forming acetic acid. The dose is given about an hour and a quarter before operation: it is run in slowly through a well lubricated catheter, about ten minutes being taken for its administration. The patient is usually drowsy or even asleep by the time the catheter is disconnected. After the operation the patient usually sleeps for some hours. Postoperative excitement seldom occurs

HOTTEN, W. I. T. Premedication in general anaesthesia *Med J Australia*, 1935, July 6, 5-12

TRICHLORETHYLENE.

Trichlorethylene, $CHCl.CCl_2$, is a strong-smelling liquid used commercially as a solvent for fats and tarry products. Therapeutically it has been given by inhalation (10 to 25 drops on cotton-wool several times daily) in cases of trigeminal neuralgia (see PRESCRIBER, 1930, Feb., 72), but so far it does not appear to have been used as an anaesthetic. STRIKER, GOLDBLATT, WARM, and JACKSON (Cincinnati) report its use in 304 cases of minor surgery and dental extraction. It afforded a satisfactory anaesthesia of several minutes, followed by quick recovery and very little after-effect. In one case an overdose caused respiratory arrest, which was overcome by artificial respiration. The type of anaesthesia resembled that from nitrous oxide or ethylene. Trichlorethylene has the advantage of *being non-inflammable.*

STRIKER, C., GOLDBLATT, S., WARM, I. S., and JACKSON, D. E. Clinical experiences with the use of trichlorethylene in the production of over 300 analgesias and anesthesias *Anesth. & Analg*, 1935, Mar.-Apr., 68-71

VINYL ETHER.

Divinyl oxide, known also as vinyl ether or divinyl ether, $(CH_2CH)_2O$, is closely related chemically to ethylene, CH_2CH_2. It is not exactly a new compound, but its use as an anaesthetic was

first suggested only some five years ago. It is a highly volatile liquid (boiling-point 28·3° C. or 83° F.), with a sweetish ethereal odour not unlike that of ethylene. It is more inflammable than ether, and in the pure state is relatively unstable, decomposing readily with the formation of formaldehyde and formic acid in presence of light and air or traces of acid. As prepared for anaesthesia it contains 0·01 per cent. of phenyl-alpha-naphthylamine to prevent decomposition, and 3·5 per cent. of absolute ethyl alcohol to prevent freezing on evaporation. It is supplied for investigational work under the name of *Vinethene.*

Vinyl ether ('vinethene') has been investigated by the Anaesthetics Committee of the Medical Research Council, whose report was cited in our review last year (PRESCRIBER, 1935, Apr., 112). The conclusions arrived at are: In animals it is a good anaesthetic with a wide margin of safety. It is highly inflammable. In man it appears to be a good anaesthetic; it is not irritating to the respiratory passages, it usually provides adequate muscular relaxation, and it shows a remarkable absence of after-effects, particularly vomiting. Owing to potency and rapidity of action great care has to be exercised to avoid overdosage.

BOURNE (Montreal), whose previous report was mentioned last year, contributes another note on its use in obstetric practice. The following are his conclusions: Used to produce anaesthesia for obstetrical procedures it does not cause liver damage, nor does it interfere with muscular activity in the intestines and in the uterus. It is particularly suitable for obstetrical anaesthesia on account of its safety for mother and child, its ease of administration, the rapidity of its action, the satisfactory maintenance of any desired degree of narcosis, and the early uneventful recovery.

DÖRFFEL (Leipzig) also reports favourably on the use of vinyl ether ('vinethene'), which he has used in 200 surgical cases.

BOURNE, W. Vinyl ether obstetric anesthesia for general practice. *J.A.M.A.*, 1935, Dec. 21, 2047-2051, *Canad. Med Assoc J.*, 1935, Dec., 629-632
DÖRFFEL, E. W. Vinethen, ein neues Rauschmittel *Dtsch med Wschr.*, 1935, June 14, 955-957.

LOCAL ANALGESIA.

In conformity with the terminology of the best authorities, the word 'analgesia' is here employed to designate those methods of producing insensibility to pain—local, spinal, regional—which do not involve loss of consciousness, the term 'anaesthesia' being limited to conditions involving unconsciousness.

ADAM advocates local analgesia for operations on the face, neck, thorax, and genito-urinary tract, especially in the presence of heart-disease, emphysema, bronchitis, arteriosclerosis, kidney disease, and impaired liver function. Fractures may be easily and painlessly

reduced by injection of 20 c cm. of pantocain (decicain) solution (0·1 per cent.) between the bone ends, which causes prompt cessation of pain and muscular contraction. Postoperative pneumonia, when it occurs after local analgesia, runs a much more favourable course than that following narcosis.

DAVIS (London) recommends the employment of local analgesia in many gynaecological operations: *the method, he says, has never* attained the popularity in this country that it enjoys on the Continent and in America. While not advocating its widespread substitution for general anaesthesia, he suggests that many minor operations may be advantageously performed by this method. Many patients are psychologically unfitted for local analgesia, but there are still many whom it would benefit.

A study of dental local analgesics by TAINTER and MOORE *(San Francisco) has yielded some remarkable results.* 'Blind tests' were made on 457 persons with various well-known analgesics and also with normal saline and dilute alcohol coloured and flavoured to resemble the analgesic solutions. In the cases where these blank control solutions were used partial or complete analgesia was apparently produced to the satisfaction of operator and patient in from 17 to 54 per cent. of the cases. Of the analgesics used, butesin (butyl-*p*-aminobenzoate), phenol, benzyl alcohol, and orthoform were effective in 75 per cent., but caused necrosis or sloughs in a few. Butyn, cocaine, saligenin, chlorbutol, and benzocaine produced analgesia in all cases, but benzocaine was found to cause sloughs in a number. These workers conclude that claims for local analgesics in the mouth must be regarded with scepticism as psychological conditions may produce apparently positive results. The low sensitivity of the gum tissues promotes the full play of suggestion, and the need for topical analgesics is limited to persons with oversensitive gums or to conditions where the need for analgesia is unusually great.

The question of premedication is discussed by CORLETTE (Sydney). When local analgesia is employed for major surgery, premedication is essential—the procedure becomes narco-local analgesia. The aims of premedication are (*a*) to remove fear and induce calm, (*b*) to dull the acuteness of pain perception, and (*c*) to dim the function of *memory. Morphine blunts the sense of pain* and hyoscine dims or obliterates the memory. The dose of morphine should be sufficient to damp down the primary excitability caused by the hyoscine and to encourage its sedative action. The doses of morphine and hyoscine vary according to the age and size of the patient. To avoid any tendency to excitement it is essential that sufficient time should elapse between the premedication injection and commencement of the operation—about an hour is the optimum period.

Butyl-para-aminobenzoate.—*This is the normal* butyl ester of para-aminobenzoic acid, and is closely related to benzocaine,

B.P., which is ethyl-para-aminobenzoate. It is known commercially as *Butesin* (Abbott) and as *Scuroform* or *Butoform* (May & Baker). Though insoluble in water it is soluble in fatty oils, a property which has recently found application for it as an analgesic in rectal surgery and skin conditions. *Scuroform Anaesthetic Compound* consists of procaine base, 1·5; scuroform, 6·0; benzyl alcohol, 5 0; almond oil to 100. *Scuroform Anaesthetic Ointment* contains the same ingredients in the same proportions, but in an ointment base instead of almond oil. Scuroform itself may be used mixed with talc, boric acid, etc., as a dusting powder or insufflation; with menthol and olive oil as a throat spray; or in various ointment combinations in dermatology.

Another preparation of a somewhat similar character is *Proctocaine* (Allen & Hanburys), which is described as an improved form of 'A.B.A.,' in which the oil soluble ingredient is butyl-*p*-aminobenzoate ('A.B.A.' contains benzocaine 3, benzyl alcohol 5, ether 10, sterilized oil to 100). Proctocaine is recommended for the same purposes—rectal surgery, anal fissure, and pruritus ani.

MORGAN (London) has found an oily solution of butyl-para-aminobenzoate very valuable in rectal surgery and in painful conditions in and around the anus The formula he gives corresponds with that of 'scuroform anaesthetic compound' mentioned above. This solution is painless on injection and has a prolonged analgesic effect due mainly to its slow rate of diffusion. If the solution is warmed and injected slowly, analgesia is almost immediate. Analgesia lasts for a period varying from seven to twenty-eight days or even longer. Relaxation of the anal musculature is greater and more prolonged than with any other solution tried, and the preparation is comparatively non-toxic. From 20 to 30 c.cm. may be injected without any local reaction. Morgan has used this solution successfully in anal fissure, pruritus ani, anal spasm, and minor rectal operations. Full details of his technique are given in the original article.

Cobefrin.—A new vasoconstrictor for use with local analgesics has been put on the market under this name. It is related to adrenaline and is soluble in water, giving a colourless and practically neutral solution. The solution must be kept in alkali-free glass. Its action is similar to that of adrenaline, but its vasoconstrictor effect is not followed by secondary vasodilatation and consequent rapid fall in blood-pressure. It is issued by Bayer in combination with procaine (novocaine) as solution (½ and 1 per cent.) and tablets. In other countries it goes by the name of *Corbasil*.

Decicain.—This is the name now given to *Pantocain*, described in last year's review. This 'Bayer' product is one of the procaine series. It is a white crystalline powder, soluble in water forming a neutral solution, which is not decomposed by boiling. A one per cent. solution in normal saline has a *p*H of 6·7 (faintly acid), while a

0 1 per cent similar solution has a *p*H of 7 (neutral) The name decicain has been given to it because in whatever manner it is used the strength required is about one tenth that of cocaine or procaine similarly employed

FLÖRCKEN (Frankfort on Main) reports on its use in surgery *A 1 1000 solution is as effective as procaine one per cent* and has as little toxicity It causes no irritation, does not destroy the red corpuscles, and may be combined with adrenaline while the analgesia comes on more rapidly and lasts longer than with procaine It has been used effectively in operations for goitre, trepanning, laparotomy, etc , while its most successful use has been in spinal analgesia It does not reduce the alkaline reserve of the blood and causes no injury to liver, kidneys or heart

Percaine (Nupercaine) —This 'Ciba' product does not belong to the procaine series, being a quinoline derivative It is a white powder, very soluble (2 in 1) in water, the solution being practically neutral to litmus As alkalis readily precipitate the free base, care must be taken to use alkali free glass in all procedures Percaine is used largely in urology and proctology, also for spinal analgesia (*q v*)

Procaine —Procaine hydrochloride is now the official name for the local analgesic known as novocaine, ethocaine, kerocaine, planocaine, etc It is the hydrochloride of diethylaminoethyl *p* amino benzoate and is a stable white powder soluble in its own weight of water It resembles cocaine in action but is less toxic Various strengths from 0 5 to 10 per cent are used according to the purpose *for which they are required Procaine hydrochloride is perhaps the* most widely used of the local analgesics

BURMEISTER (Cincinnati) offers a method whereby a buffered isotonic solution of procaine hydrochloride for use in dentistry may be obtained To the requisite amount (0 1 gm) of procaine hydrochloride crystals add 5 c cm of the following solution sodium chloride 7 0 , sodium phosphate (Na_2HPO_4), 1 7 , potassium acid phosphate (KH_2PO_4) 0 2 , water (double distilled) to 1000 On solution there will be ready for use 5 c cm of a sterile buffered isotonic 2 per cent solution of procaine hydrochloride with a *p*H value of 7 3 to 7 6 If desired one minim of 1 1000 adrenaline *solution may be added*

A 2 per cent solution of procaine hydrochloride is recommended by SPERBER and SABATINO (New York) for injection in cases of sprained ankle From 4 to 8 c cm is introduced into the painful periarticular area after skin sterilization Relief of pain is instantaneous, return of function is prompt, and oedema disappears rapidly No re injections are necessary and there is no period of disability In articular trauma, it is explained, there is no lesion of the ligaments, only the nerve endings being damaged, and the procaine blocks these and stops abnormal excitation

Saligenin.—Saligenin (or more correctly saligenol) is salicyl alcohol or *o*-hydroxybenzyl alcohol, $C_6H_4(OH).CH_2.OH$, the alcohol of which salicylic acid is the corresponding acid. It is by no means a new discovery, having first been obtained in 1845 by the action of emulsin upon salicin. It has been used internally as a remedy for rheumatism, and its use as a local analgesic was mentioned in these pages fifteen years ago (PRESCRIBER, 1921, Mar., 153). Its use in this respect has recently been revived by the COUNCIL ON DENTAL THERAPEUTICS of the American Dental Association. It occurs as white crystals or crystalline powder, soluble in water forming a neutral solution. Its action is similar to that of procaine hydrochloride, and it is said to be as effective as procaine and much less toxic. As the analgesia lasts longer the addition of adrenaline is not necessary. In infiltration analgesia the dosage is the same as for procaine hydrochloride.

ADAM, L. Some principles of local anaesthesia *Surg Gyn & Obstet*, 1935, Mar., 675-679
BURMEISTER, C. H A practical method for the extemporaneous preparation of a buffered anesthetic solution *J Amer Dent Assoc*, 1935, Sept., 1514-1520
CORLETTE, C. E. Premedication for local anaesthesia. *Med J Australia*, 1935, July 6, 1-5.
COUNCIL ON DENTAL THERAPEUTICS. Topical anesthetics with reference to saligenin. *J Amer Dent Assoc*, 1935, Sept, 1589-1591
DAVIS, A. A. Local anaesthesia in gynaecology *B.M J*, 1935, Mar. 30, 636-638.
FLÖRCKEN, H. Erfahrungen mit dem Pantocain in der Chirurgie *Münch med Wschr*, 1935, Jan 17, 92-94
MORGAN, C. N. Oil-soluble anaesthetics in rectal surgery *B M J*, 1935, Nov. 16, 938-942
SPERBER, P., and SABATINO, N A. A new treatment for sprained ankle. *Med Record*, 1935, Nov 20, 469, *Med World*, 1936, Feb 7, 764-766
TAINTER, M L, and MOOSE, S M Studies in topical anesthesia 1. The efficacy of certain common anesthetics when used on the gums. *J Amer Dent. Assoc*, 1936, Feb, 244-250

SPINAL ANALGESIA.

In a general review of the subject, DOYLE (Melbourne) states that the main advantage of spinal analgesia is that it provides a complete relaxation of the abdominal muscles and blocks all passage of nervous impulses from the area of operation to the cerebrum. Contraindications are (*a*) cardiovascular — low blood-pressure, anaemia, angina, coronary thrombosis, (*b*) nervous, and (*c*) septic conditions of the spine and the height of the operative field. The general indications are any operation below the umbilicus which, by reason of its severity, is likely to produce a condition of surgical shock, or where in such an operation general anaesthesia is likely to lead to pulmonary, cardiac, or renal complications. He recommends a form of procaine known as 'neocaine' (Anglo-French Drug Co.) and gives details of technique.

A simular review of the subject is given by STEIN and TOVELL

(Mayo Clinic), who conclude that properly induced spinal analgesia produces complete freedom from pain in the operative field, and relaxation of the muscles Operative exposure is facilitated The maximal fall in blood-pressure occurs early in the operation, when the patient is best able to withstand it Mucous membranes are not irritated as with ether, and postoperative vomiting is minimal The method may be used for patients requiring emergency surgical procedures but who have slight infection in the upper part of the respiratory tract The method has its limitations The patient is awake and may fail to cooperate Nausea and vomiting during operation may necessitate the administration of supplementary general anaesthesia With the use of procaine, there is a definite limit to the duration of analgesia For operations in the lower abdomen exceeding one hour in duration, satisfactory analgesia may be obtained by a mixture of decicain and procaine For lengthy operations in the upper abdomen supplementary general anaesthesia is advised Puncture headache is unpleasant, and treatment is not entirely satisfactory, stay in the hospital may be prolonged, but ultimate relief is assured The incidence of such headache in their series was 6 6 per cent

Recording his experience of 500 cases, DORLING (Tientsin) deals, among other things, with complications Headache, he says, is rare when a fine needle is used and a very small amount of cerebro spinal fluid is withdrawn before the injection Retention of urine is common when amylocaine is used, but is seldom seen after procaine Fall of blood-pressure is not dangerous in low spinals, ephedrine given immediately after the spinal injection, and the *assumption of the Trendelenburg position after ten minutes*, counteract it

Describing his experience of spinal analgesia during seven years of private practice, WOOD (Ottawa) says that it gives the best opportunity for atraumatic surgery The traumatic shock is lessened at its origin, and is blocked at the spinal nerve roots and so does not reach the cerebral or spinal centres Nausea is practically eliminated Postoperative distension is very greatly reduced Patients who have had both general and spinal anaesthesia and come to a further operation, frequently demand to have the spinal method repeated

Percaine —The use of percaine for spinal analgesia had a warm advocate in W Howard Jones, whose lamented death in July last means a loss to surgery Jones introduced what is known as the 'hypobaric' solution of percaine This drug, being powerful, is efficient in very high dilutions—1 2000, 1 1500, and 1 1000—the duration of analgesia being proportional to the concentration The medium strength, 1 1500 in 5 per cent saline (dose 10 to 20 c cm), is most suitable for the average case The modification of Jones's method, introduced by Sebrechts, and the technique of Quarella, were described in last year's review

TREMPE (Quebec) has used the Howard Jones method in 800 spinal analgesias The arterial pressure of the patient is taken the day before the operation A systolic pressure of 110 or less is regarded as a contraindication No premedication is necessary, but an injection of ephedrine, ½ grain, is made ten or fifteen minutes before operating, in order to prevent fall of blood-pressure The spinal injection must be made very slowly to avoid a too rapid distension of the dural sac, which may be a cause of headache The solution should be at body temperature when injected Trempe injects not more than 15 c cm of the 1 1500 solution between the first and second lumbar vertebrae The head and trunk should never be higher than the rest of the body, the solution being hypobaric Trempe has never met with any serious sequelae

A new technique of spinal analgesia with percaine was described by WILSON in 1934 The principle involved is to allow a light (hypobaric) solution of percaine to ascend the vertical spinal canal, timing it to reach certain levels The rate of ascent of a hypobaric solution in a normal vertical spinal canal is the same as in a glass tube of the same length and bore containing cerebrospinal fluid Wilson says that it does not seem possible that a light solution like percaine can ever reach the higher subarachnoid spaces by direct ascent He is convinced that after the adoption of the Trendelenburg position it is quite impossible for the light mixture of percaine and cerebrospinal fluid, which has been allowed to ascend to a certain level beforehand, to diffuse any higher Absorption of percaine solution takes place during the whole time that it is ascending the canal, and the amount therefore decreases as it ascends With the vertical technique, using slowly injected percaine, a steadily rising and well mixed area travels up the whole length of the spinal canal to the level required without setting up currents, which are bound to occur in rough and uncontrolled injections

ANDREASON (Jhelum, India) reports trials of this method in a number of cases, giving full details of his method of working His average doses and times for operations of about one hour were low—10 c cm of percaine solution, the patient remaining upright for twenty seconds, medium—12 c cm, thirty seconds upright, high—15 c cm, forty seconds upright After that the patient is put in the Trendelenburg position Much smaller quantities of percaine are required by this method, and consistently good results are obtained if the technique is carefully followed He gives a record of fourteen cases anaesthetized by this method, 1 1500 solution of percaine being used in all cases

Complications—BROCK, BELL, and DAVISON (New York) record seven cases of nervous complications following spinal analgesia In one case tissue changes in the spinal cord were observed The symptoms included meningitis, cauda equina neuritis, polioencephalitis, radiculitis, and severe toxic myelopathy Two

proved fatal; one developed diabetes; the others recovered either completely or with some residual signs. The drugs used were: a preparation of procaine and strychnine sulphate (two cases); percaine (three cases); procaine hydrochloride (one case); drug unknown (one case). These workers emphasize the comparative rarity of such sequelae and assume the existence of tissue sensitivity to the drugs used. Unfortunately there is no way at present of learning beforehand whether or not a patient's nervous tissues are oversensitive to these drugs.

Therapeutic Applications.—*The use of spinal analgesia as a* therapeutic agent in relieving intestinal stasis has already been referred to in these reviews (see PRESCRIBER, 1933, Apr., 135; 1935, Apr., 124). A case in which anuria was relieved by this means is reported by HAYES and PARAMORE (Rugby). A man, aged 25, had been operated on for appendicitis and the wound proved difficult to heal, the abdomen being distended and vomiting frequent. In addition to bowel obstruction the patient developed anuria, the result, it is believed, of the straining and vomiting and consequent block in the renal circulation. Spinal analgesia with tropacocaine was *tried and considerable improvement resulted. Twelve hours* later a second spinal injection was given. The result is described as 'magical': the patient's condition steadily improved from that time onward. The result is attributed to the action of the spinal injection in reducing the blood-pressure and assisting peristalsis.

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BROCK, S., BELL, A., and DAVISON, C. Nervous complications following spinal anesthesia: a clinical study of seven cases, with tissue study in one instance. *J.A.M.A.*, 1936, Feb. 8, 441-447
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HAYES, D. S., and PARAMORE, R. H. Anuria treated with spinal anaesthesia *Lancet*, 1935, Sept. 7, 554-556
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WILSON, W. E. Intra-thecal nerve root block: some contributions and a new technique *British J. Anaesth.*, 1934, Jan., 43-55, *Proc. Roy. Soc. Med.*, 1934, Feb., 323-331
WOOD, E. H. Seven years of spinal anaesthesia in private practice *Canad. Med. Assoc. J.*, 1935, Sept., 298-302

Haemorrhage: Congo Red.—NIKOLAIEW and GUREWITSCH report that intravenous injections of congo red (10 ml. of a one per cent. solution) are useful in gynaecological haemorrhages of an inflammatory nature. It accelerates coagulation and increases the number of thrombocytes.—*Zentralb. f. Gynäk.*, Nov. 2, '35, p. 2672.

New Drugs and Preparations.

[Under this heading are given brief notices of new non secret products as they appear on the market or are mentioned in medical literature The notes are intended for reference only, and must not be taken to imply anything in the nature of a recommendation In most cases the information is derived wholly or mainly from makers advertisements]

Antemin —Tablets containing cerium oxalate for treatment of vomiting of pregnancy and travel sickness (H K Labs , London)

Arthrytin —The calcium salt of *o*-iodoxybenzoic acid (see PRESCRIBER, 1928, Sept , 301) used in the treatment of arthritis In tablets of 7¾ grains (0 5 gm) for oral administration , also the ammonium salt (powder) for intravenous injection (May & Baker Ltd , Dagenham)

Betaxin —A preparation of vitamin B_1 (antineuritic vitamin) in aqueous solution for parenteral administration Ampoules of 2 c cm contain 400 pigeon units (a unit is the amount that cures in one day a pigeon suffering from beri beri) Indicated in beri beri, also found by Neumann (*M m W*, Dec 6, 35, p 1959) to be of value in degenerative lesions of the spinal cord Still in the experimental stage (Bayer Products Ltd , London)

Brom-Nervacit —A nerve sedative containing potass bromide, sodium phosphate, barbitone phenazone, and flavourings For treatment of nervous disorders Dose one tablespoonful morning and midday and two tablespoonfuls in the evening (Brom Nervacit Ltd , London)

Calcidrine Syrup —Contains in each fluid ounce calcium iodide, 7 grains , ephedrine hydrochl , ⅛ grain , codeine sulphate ¼ grain , nembutal, ⅛ grain , syrups of wild cherry and tolu For treatment of cough (Abbott Labs Ltd London)

Calsoma —The tribasic phosphates of calcium and magnesium in effervescent form Neutralizes excessive gastric acidity without producing alkalinity (Abbott Labs Ltd , London)

Climatone —Tablets containing ovarian hormone, theobromine calcium lactate, etc , for relief of menopausal hypertension and psychic and congestive conditions occurring at the menopause (Paines & Byrne Ltd , Greenford)

Collopyrin —Formerly ' kaopyrin ' this is a combination of acetyl salicylic acid and collosol kaolin analgesic, antipyretic and antirheumatic In tablets (British Colloids Ltd , London)

Festan —A preparation of the three chief pancreatic ferments lipase, amylase, and protease, also an enzyme capable of disintegrating cellulose called hemicellulose Indicated in cases where digestive disturbance is due to fermentative insufficiency (Bayer Products Ltd , London)

Fissan —Under this name is introduced a series of skin preparations containing ' fluoro silica colloid ' (an exceedingly light powder) and lactalbumin The series comprises dusting powders, lotion paste (zinc oxide) basic ointment variously medicated emulsion, anal ointment, and suppositories For treatment of skin and anal affections (Genatosan Ltd , Loughborough)

Genora.—A vaccine for oral administration for the prevention of colds, influenza, and pneumonia Contains *B influenzae* (Pfeiffer), pneumococci (several types), influenza streptococcus (Thomson) haemolytic streptococci, *M catarrhalis*, and *Anaeromyces bronchitica*, 2000 million organisms per c cm Prepared by the Pickett-Thomson Research Laboratory, and described by Thomson, Thomson, and Thompson *B M J*, Feb 8, '36, p 258 (Genatosan Ltd , Loughborough)

Iodo-Ray Sterules.—Glass capsules containing a solution of sodium ortho-iodohippurate (see PRESCRIBER, 1934, Jan , 35) for radiographic purposes In two varieties *intravenous*, containing 15 gm in 23 c cm , and *retrograde*, containing 3 gm in 10 c cm The intravenous variety may be used also for oral administration in excretion urography (W Martindale, London)

Ipral-Sodium.—Sodium ethyl-isopropylbarbiturate Used as a hypnotic Dose, 2 to 4 grains (0 12 to 0 25 gm) followed by a draft of hot liquid (E R Squibb & Sons, New York)

Leucotropin.—A solution of phenylcinchonate of hexamine, given by intravenous and intramuscular injection in rheumatic affections and inflammatory conditions Ampoules, 5 and 10 c cm (Silten Ltd. London)

Mapharsen.—The hemi-alcoholate of 3 amino-4 hydroxyphenylarsine oxide hydrochloride (29 per cent As) Said to be particularly efficacious in early syphilis and to give less severe reactions than arsphenamine Soluble in water Dose, intravenously, 0 03 gm for women and 0 04 gm for men, gradually increased (Parke, Davis & Co , London)

Multivite Pellets.—Each chocolate-coated pellet contains vitamins A (3000 international units), D (600 units), and C (100 units), with a proportion of vitamin B complex equivalent to 2 gm yeast Designed as a general tonic and for increasing resistance to infection (The British Drug Houses Ltd , London)

Novurit.—A complex organic compound of mercury, with theophylline, in 10 per cent solution for intravenous or intramuscular injection as a diuretic It is also given as suppositories containing 0 5 gm (Parkinson and Thomson *Lancet*, Jan 4, '36, p 16), acting well in patients with cardiac oedema in whom injection is not suitable (W Martindale, London)

Ostomalt.—A malt preparation containing vitamins A, B, C, and D, flavoured with orange (Glaxo Labs , Greenford)

Perparine.—A synthetic alkaloid (quinoline derivative) analogous to papaverine, indicated in spasmodic conditions of smooth muscle In tablets (0 04 gm hydrochloride) for oral use, and in ampoules (1 1 c cm containing 0 04 gm) for injection (Agents Reitmeyer Calburn & Kindersley Ltd , London)

Petein.—A new vaccine for whooping-cough, containing about 60 different strains of bacteria collected in recent epidemics and cultivated on fresh blood media, concentrated, detoxicated, and standardized Used both in treatment and in prophylaxis , given by intramuscular injection One course, consisting of four injections (0 25, 0 5, 0 75, and 1 0 c cm) during seven days, is said to be sufficient In bottles containing four injections (2 5 c cm) for one course (Schering Ltd , London)

REVIEWS OF BOOKS.

Aggressive Medicine By John Maberly, M R C S, L R C P Pp 232 (Bailliere, Tindall & Cox 10s 6d)

The title of this book is rather intriguing and a perusal of its contents removes any doubt of its real meaning, for one finds that it is concerned with the clinical results attending the use by the author of iodized tincture of guaiacol and tincture of guaiacol chloriodide, also of *Monsonia ovata* Wonderful results are claimed in many diverse diseases, such as erysipelas, rheumatic fever, meningitis, asthma, diphtheria, typhoid, scalds and burns, and high blood pressure, to mention some of them In the author's hands success would appear to have been invariable, and one would like to wait the experience of other clinicians with these preparations before offering any comment—confirmation would of course be important in helping to establish the author's thesis J O

A Synopsis of Physiology By A Rendle Short, M D, F R C S, and C I Ham, M B, B Ch, F R C S Ed Second Edition Edited by C L G Pratt, M D Pp 312 (Wright 10s 6d)

At first sight the second edition of this work seems only half the size of the first, but closer inspection shows that it actually contains about fifty pages more, thinner paper being responsible for the apparent reduction This is all to the good, for in works like this which are used for study and reference bulk is a drawback The original authors have retired from active teaching and it became necessary to enlist help for the revision, which has been undertaken by Dr Pratt Very complete revision is evident on nearly every page, such subjects as endocrines and vitamins showing almost entire recasting The work is on lines similar to the others of the series it is a condensed textbook in which the basic facts are summarized with great skill

MEDICAL RESEARCH COUNCIL SPECIAL REPORTS

No 205 *The Source of Infection in Puerperal Fever due to Haemolytic Streptococci* By Dora C Colebrook, M D (H M Stationery Office 1s 6d)

Puerperal sepsis is one of the problems of medical science it is known to be due to a haemolytic streptococcus, but this organism comprises a number of groups having different properties Dr Colebrook has studied a large series of cases of puerperal fever in their bacteriological aspect, and she has been able to indicate with a high degree of probability the usual sources, outside of the genital tract, from which haemolytic streptococci may be conveyed to the patient It is of interest to learn that the respiratory tract is at least one frequent source of this infection The work was done in the research laboratories of Queen Charlotte's Hospital, London

No 206 *The Bacteriological Grading of Milk* By G S Wilson, M D, and others Pp 392 (H M Stationery Office 7s 6d)

In this report Professor Wilson and his assistants at the London School of Hygiene and Tropical Medicine give an account of a critical inquiry into the validity of the methods available for the bacteriological grading

of milk The investigation occupied three years and its cost was met by grants from the Empire Marketing Board and the Ministry of Health The objects of the investigation were to ascertain the relative value and precision of the current procedures and to define a simple test by which the grading of milk in terms of its living bacterial content can be reliably performed It is claimed that these objects have been successfully attained The general conclusion is that a modification of the methylene blue reduction test is the best for the purpose The subject is very exhaustively dealt with in the report

A CATALOGUE OF BRITISH MEDICAL FILMS has been published by the British Film Institute, 4 Great Russell Street, London, W C 1, at one shilling The films are classified in accordance with the medical curriculum particulars being given of the author, width of film, silent or sound, length, suitability, and name and address of owner A full index is appended Those who desire to use films for educational or lecture purposes are enabled, by means of this catalogue, to get in touch with the owners with a view to hire loan, or purchase

A DICTIONARY OF RELIGION AND RELIGIONS, by Richard Ince, M.A (Barker, 9s), contains a number of items of medical interest, such as psychology, psycho analysis, psychotherapy, faith healing, etc Under Christian Science the author tells us that its practitioners 'claim to be able to cure any and every disease from toothache to cancer by prayers for which a regular fee is charged' There is much interesting reading in the book, including definitions of many theological and ecclesiastical terms and a concise account of the principal religions of the world

STORM IN A TEACUP is the title of James Bridie's latest play (Constable, 2s 6d) It is not exactly a new play, but a rather free adaptation to a Scots setting of Bruno Frank's 'Sturm im Wasserglas' Dr Mavor's touch is recognizable in the various characters which are sketched with skill, and while the play is almost pure farce it is clever farce and shows that 'sense of the theatre' which many of our modern playwrights lack It is hardly the best that this author has given us—we prefer some of his earlier works—but it is good entertainment and it reads as well as it acts Being a translation, it gives the author no opportunity for the unconventional excursions of some of his recent works, but in so far as it is pure Bridie it is worthy of him

In MEDICAL AND OTHER VERSES (H K Lewis, 3s 6d), Mr A E Roche has collected in a little volume of 92 pages some of his youthful effusions He modestly—and perhaps wisely—refrains from calling it 'poetry,' and like most such collections the merit of the pieces varies The humorous verses lack the easy lilt necessary for their full effect, but his serious pieces move more smoothly and some of them are distinctly poetic in their fancy The book concludes with some clever translations of bits from Latin and Greek classics

PATHOLOGICAL ARCHITECTURE.—'Na, na,' said the stone cutter, 'oor wark isna' what it was What wi' tubercular scaffoldings and sympathetic stone, a mason's job isna' worth a damn!'

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ENDOCRINOLOGY: SIXTEENTH SPECIAL NUMBER

(SIXTH OF NEW SERIES)

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ENDOCRINOLOGY: A YEAR'S PROGRESS.

FOR the sixteenth year in succession it is our privilege to present a review of the progress of endocrinology during the preceding twelve months. As time goes on the amount of literature to be reviewed increases, making selection by no means easy, but the present issue may be said to contain every advance of importance down to the time of going to press.

Among the mass of information presented, one or two points stand out as of special interest. It has been observed that parathyroid tumours occur more frequently in countries where sunshine is less abundant. Ultraviolet rays stimulate the formation of vitamin D, lack of which has an unfavourable influence on the calcium metabolism, putting an extra strain on the parathyroids. Another point is that better knowledge of glandular interrelationships is helping to place pluriglandular therapy on a sounder basis as distinguished from mere 'shot-gun' treatment. One of the leading endocrinologists of America admits that when stimulating action is required a small dose of thyroid may advantageously be added to any glandular medication.

The position of the pituitary in relation to the other glands is becoming more clearly defined. Though still regarded as the 'master gland,' its position is that of a leader—*primus inter pares*—whose success depends upon the respect and co-operation of those he leads. It is when the leader loses his head and becomes dictator that the trouble begins.

The department of endocrinology showing the greatest advances is that dealing with the sex hormones. Here

biochemistry has rendered notable service to medicine The chemical constitution of oestrone is now known, and its close similarity not only to the male hormone androsterone but also to the vitamins and to certain carcinogenic substances has opened an avenue for research that should lead to important discoveries Clinical application of the female hormones is advancing slowly but on sure ground Oestrone and oestradiol are definitely known to be of value in menopausal symptoms, and good results have followed their use in gonococcal vaginitis in children, this application being based on sound reasoning The hormone of the corpus luteum, progesterone, has found application in cases of habitual or threatened abortion, as also in certain types of dysmenorrhoea

Perhaps the most promising field lies in the clinical use of the gonadotropic hormones of the anterior pituitary Commercial production of the actual hormones from the gland itself has so far not proved satisfactory, and the separation of the two hormones concerned (prolan A and B) has as yet eluded the skill of the biochemist The urine of pregnancy, however, contains both hormones, and has proved a satisfactory source for their extraction, but for the present these can only be known as 'anterior pituitary-like' products as they are believed to be different from the hormone as contained in the gland They have been standardized, and their use is now fully appreciated

The position in regard to the male hormone is less definite Much work has been done and great advances have been made, but not to the extent of defining its clinical application beyond a very limited field What is wanted is an endocrine product that will be effective in male senile conditions, such as enlarged prostate and the male climacteric, and it is possible that such an application may be found in time Meanwhile physicians must wait patiently for developments which are almost certain to come

Other advances to which attention may be directed include a better acquaintance with the functions of the adrenal cortex, further study of the anterior pituitary interrelationships, and a suggestion that the pineal gland is a kind of junior partner to the pituitary These are only a few of many points of interest to be found in the following pages, perusal of which we commend with confidence to our readers

THE EDITOR

THE THYROID GLAND.

FROM the earliest days the thyroid gland was recognized as an entity by anatomists, though for centuries its physiological significance remained a puzzle For a time it was believed to have some relationship to neighbouring organs such as the larynx, and it was not until the end of the nineteenth century that the recognition of the separate identity of the parathyroids led to a clearer understanding of the function of the thyroid To day a fuller knowledge of other endocrine glands has somewhat discounted its relative importance, though it is still the gland about which most is definitely known

Anatomy.—The thyroid and parathyroids form a group of glands, which while anatomically related differ entirely in function and physiological relations The thyroid gland is situated in the lower part of the neck and consists of two lobes, one on each side of the larynx, connected by a transverse isthmus The weight of the whole thyroid in man is from 20 to 25 grammes and the average length of each lobe is 5 6 centimetres (2 to 2½ inches), though its size varies in different individuals, the gland is larger in women than in men About 75 per cent of the gland consists of water The vesicles of which it is composed are filled with a viscid fluid called the 'colloid' This contains the active principles of the thyroid secretion, the iodine containing hormone

A study of the histology of the thyroid gland in senescence is reported by DOGLIOTTI and NUTI (Univ of Florence, Italy) They find that in old age the gland undergoes profound structural modifications indicative of overfunction The augmented thyroid secretion is regarded as a compensation for the senile decline of metabolism

The presence of accessory thyroid glands has occasionally been reported (see PRESCRIBER, 1932, May, 151) Recently D'ABREU (Cardiff) has studied the behaviour of misplaced thyroid tissue and describes three cases of lateral aberrant thyroids He finds that the pathological changes in these cases are very different from those of aberrant thyroid tissue found in a superior or inferior position Symptoms of hypothyroidism after removal are unknown, and the cases are thus in contrast with those of superior aberrant thyroid where such symptoms are not uncommon Clinically the condition is not usually diagnosed until operation The most important diagnostic appearance is the bluish-black colour, and unless this is known the surgeon may regard the condition as a melanotic growth If such tumours are seen, careful and complete extirpation is essential because of the danger of their becoming malignant The prognosis is doubtful and all cases must be carefully followed up

Physiology.—The thyroid gland serves to regulate the basal metabolism Deficiency of thyroid secretion (hypothyroidism) manifests itself in lowered basal metabolism and a general slowing

down of the human machine, mentally and physically The pulse becomes slower, fatty tissue accumulates, and the condition known as myxoedema is observed Administration of thyroid gland substance remedies this condition In the case of excessive thyroid secretion (hyperthyroidism), mental and bodily activity is increased, the basal metabolic rate rises the individual uses up his stores of fuel and becomes thin and the heart rate increases

In young and growing persons the thyroid gland exercises a regulating effect on growth both mental and physical Children in whom deficiency of the thyroid is congenital are called *cretins* The activity of the thyroid is closely associated with the metabolism of iodine, of which the thyroid secretion contains a large proportion, and the thyroid deficiency known as simple goitre is believed to be in some measure the result of a deficiency of iodine intake

In addition to its immediate effect on the metabolism the thyroid has other and less direct influences During the past few years certain interrelations with other glands have come to light, and although these are as yet imperfectly understood mention of them may be made It is definitely known that the anterior pituitary has a stimulating effect on the thyroid and it is believed that the thyrotropic factor in the pituitary plays a part in the production of exophthalmos in Graves's disease A relationship between the thyroid and the gonads has long been known to exist, as the thyroid enlarges during menstruation and pregnancy and it is probable that this interaction is effected through the medium of the anterior pituitary (MARINE) It is evident that a proper balance between the thyroid and the gonads is essential to the optimal performance of the sexual and reproductive functions Thyroid therapy has been found to correct certain disturbances of pregnancy and menstruation when these are associated with hypothyroidism

Interactions have been demonstrated also between the thyroid and the liver, the adrenal cortex the thymus and the kidneys It was shown some years ago by GERLEI that excessive thyroid feeding reduced the glycogen store in the liver, but this was believed to be due to increased utilization rather than to impairment of storage capacity Recent work by MAGISTRIS shows that the thyroid prevents the formation of glycogen in the liver, and that this action is inhibited by the anterior pituitary A relationship between the adrenal cortex the thyroid hormone and nitrogen metabolism has recently been demonstrated by KOELSCHE and KENDALL, who show that the cortical hormone exerts a protective action against the effect of thyroxine in producing a negative nitrogen balance

A relationship between the thyroid gland and haematopoiesis has been demonstrated by SHARPE and BISGARD (Omaha) The close similarity between chronic lymphatic leukaemia and the exophthalmic type of hyperthyroidism the excess of lymphocytes in the thyroid vein over those in the thyroid artery, the cure of a case of lymphatic leukaemia by total ablation of the thyroid and the development of anaemia in spontaneous and postoperative myxoedema led

them to study the question experimentally. They found that removal of the thyroid gland in rabbits produced a moderate and persistent anaemia of the macrocytic type, with a slight transient decrease of the white cell count. They are now experimenting with the effect of thyroid feeding on the anaemia.

Thyroid Disorders.—Apart from actual diseases affecting the thyroid gland, such as cancer, tuberculosis, and the like, disorders of the thyroid are associated with either under- or over-functioning of the gland itself — hypothyroidism or hyperthyroidism. The importance of early recognition of thyroid dysfunction has led to the introduction of various diagnostic tests, of which the following are the more important.

Basal Metabolic Rate (B.M.R.).—As the thyroid controls the basal metabolism, measurement of the basal metabolic rate will give an indication of the gland's activity. Basal metabolic rate means the rate of energy exchange in the body as seen under basal conditions, that is, after elimination of such factors as movement, digestion, etc. To obtain these conditions the patient must be quiet, physically and mentally, for some time before and during the estimation. Internal activity is measured in terms either of heat (direct calorimetry) or of oxygen combustion (indirect calorimetry). Direct calorimetry requires expensive apparatus and elaborate technique; indirect calorimetry may be carried out by means of comparatively simple apparatus, and consists in measuring the oxygen consumption of the patient during a given period. Air plus oxygen is rebreathed in a closed-circuit apparatus in which the exhaled carbon dioxide is absorbed; the diminution in volume of the gas indicates the amount of oxygen consumed by the patient in a certain time; in other words, the rate at which basal metabolism proceeds. Results are expressed as *plus* or *minus*; the normal B.M.R. being from plus 10 to minus 10. In hyperthyroidism the B.M.R. is above normal, in hypothyroidism it is below normal. Administration of thyroid, thyroxine, or dinitrophenol raises the rate, while iodine and its compounds reduce it.

Goetsch's Adrenaline Test.—The sympathetic nervous system is specially sensitive to adrenaline in cases of hyperthyroidism, while in hypothyroid cases sensitiveness is diminished. The test consists in the hypodermic injection in the deltoid region of 0·5 c.cm. of adrenaline solution, after which the blood-pressure, pulse-rate, and respiration rate are carefully recorded at intervals over a certain period. The reaction is positive—rise of pressure and increased pulse and respiration rate—in hyperthyroidism and negative in hypothyroidism, but it gives doubtful results in borderline cases.

Bram's Quinine Test.—This test is based on the principle that hyperthyroid patients are exceptionally tolerant of quinine. A dose of 10 grains of quinine hydrobromide is given three times daily. If the thyroid is normal the patient will show signs of cinchonism after four or five doses, or even sooner. If hyperthyroidism is

present, however, the drug may be given for a long period without any sign of cinchonism developing

Bram (Philadelphia) has reported recently that in an experience of over 4000 cases the quinine test has proved a reliable guide in diagnosis It does not discriminate between toxic adenoma and Graves's disease, but neither does the B M R Occasionally a quinine negative patient has been encountered who showed typical Graves s disease, but in such cases it has always been found that hyperthyroidism was absent and that the B M R was normal

Reid Hunt's Acetonitrile Test—Acetonitrile, or methyl cyanide, CH_3CN, when ingested acts as a poison, hydrocyanic acid being formed in the body Hunt found that mice fed with thyroid developed a remarkable resistance to such poisoning and he believed that instead of forming hydrocyanic acid the acetonitrile was oxidized by means of the thyroid to harmless formic acid and thiocyanate This forms the basis of the Reid Hunt test mice injected with the blood of a hyperthyroid patient become immune to poisoning by acetonitrile

Wokes (London) finds as the result of trials that the susceptibility of mice to acetonitrile poisoning, and the degree of protection afforded by thyroid, are both affected by the temperature at which the mice are kept At 38° C (100 4 F) the average lethal dose is about one fifth of that at room temperature, and practically no protection is afforded by thyroid This militates against the usefulness of the test as a quantitative method of assay

Wiesbader (New York) has studied this reaction in the light of recent work on interrelated glands He finds that the resistance of mice to acetonitrile poisoning is increased by the serum of pregnant women, by the anterior pituitary like hormone from pregnancy urine, and by the thyrotropic hormone of the anterior pituitary

Fellinger and Höchstädt (Vienna) in another study of this reaction, report that it may be rendered inactive by the antithyroid substance (thyroid katechin) of Blum The antithyroid substance, however, seems to act more powerfully against the thyroid itself and against the thyrotropic hormone of the pituitary than it does against thyroxine

Electrical Method—The electrical method of diagnosis devised by Brazier (London) was described in last year s review Brazier found that the 'condenser value of the skin varies in thyroid disease in such a way as to be of diagnostic value In constant current work the impedance (resistance due to self induction) is measured by resistance only, but with alternating currents the body-functions act as both resistance and condenser The ratio of these two factors is called the 'impedance angle, and it is this which shows variations in thyroid disease An apparatus has been devised which will measure this factor and give direct readings with very little disturbance to the patient In thyrotoxicosis the impedance angle (I A) shows considerable increase above normal—the severer the disease the higher the I A In non toxic goitres the I.A is

lower than normal, and is very useful in the detection of early symptoms.

BARNETT and BANGO (Brooklyn) find that the constancy of the I.A. is affected by certain factors, one of these being the state of muscular tension. They describe a phase meter which gives constant values irrespective of changes in muscular tension. In a case of pituitary dwarfism and in nine cases of pituitary deficiency the I.A. followed a fluctuating course.

HORTON, VAN RAVENSWAAY, HERTZ, and THORN (Boston) have evolved a technique for the determination of the internal impedance as apart from that of the surface. They say they have been unable to confirm many of Brazier's findings. The internal impedance for any normal person remains remarkably constant, varying but little after food, exercise, and other factors that influence the B.M.R. Using this technique they found that most untreated thyrotoxic patients had low impedance values, while untreated myxoedematous cases showed high values. Patients under treatment show marked alterations in the B.M.R. but little difference in impedance values, and it is concluded that, compared with the B.M.R., impedance values have little significance in the estimation of thyroid activity.

Other Tests.—Reporting on laboratory tests generally, MAHON (Dallas, Texas) reviews some of the tests that have been advocated, such as blood-cholesterol, blood-iodine, and sedimentation rate. He finds that none of these gives satisfactory results and he regards the B.M.R. as the only really reliable method.

Thyroid Diseases in Children.—Discussing disorders of the thyroid occurring in children, COCKAYNE (London) mentions cretinism and hypothyroidism as the commonest, both of which require treatment with small doses of thyroid. Juvenile myxoedema (complete cessation of thyroid secretion) is rare: thyroid must be given with caution. Severe thyrotoxicosis is rare, but a mild degree is not uncommon: mild cases may recover with rest and quiet assisted by Lugol's iodine solution, but severe cases may call for operation. In the goitre of puberty, which is not uncommon, small doses of iodine or iodide may be given, but the enlargement usually subsides as puberty becomes established.

Hypothyroidism.—Varying degrees of hypothyroidism are met with, from slight symptoms of deficient secretion to its complete absence, as in myxoedema. The skin is dry, with absence of perspiration; the hair tends to fall out and the outer third of the eyebrow is devoid, or almost so, of hair. The skin is pale, the face more or less expressionless, and the patient puts on fat as the result of deficient oxidization. Hypothyroid patients feel the cold intensely and usually have a subnormal temperature; they are languid, easily tired, and disinclined for physical or mental exertion. Fully developed hypothyroidism is unmistakable, but the early signs of incipient hypothyroidism are difficult to recognize. Small doses of thyroid are often effective in relieving symptoms not at first ascribed to thyroid deficiency.

An analysis of fifty three cases of mild or moderate hypothyroid ism is reported by SEWARD (Roanoke Va) The vagueness of the symptoms was in contrast to the definite symptoms of myxoedema Most of the patients were between 30 and 49 years of age and a constitutional factor seemed to play a greater part than infection in the aetiology The most important constant symptom was fatigue on mental or physical exertion, other symptoms were mental *depression irritability, insomnia palpitation, and vague joint and* muscular pains Low B M R was a constant find ng on this the diagnosis ultimately rests In some cases a mild anaemia was present Treatment consists of oral administration of thyroid and the main tenance of a cheerful disposition

The subject of myxoedema is dealt with at some length by DE WESSELOW (London) Fully developed myxoedema is relatively rare, but many degrees exist between it and mild hypothyroid sm Five main groups of hypothyroidism are recognized (1) spontaneous myxoedema, (2) traumatic hypothyroidism, (3) exhaustion follow ing on hyperthyroidism, (4) pituitary hypothyroidism (5) that resulting from local lesions of the thyroid In cases of fully developed myxoedema diagnosis is simple and if any doubt exists the B M R will afford confirmation In minor degrees of thyroid inadequacy the diagnostic value of the B M R is limited as a low rate occurs in other conditions besides hypothyroidism Dry thyroid is the main standby in treatment thyroxine does not seem to give the same result Small doses (½ grain daily) should be given at first increasing gradually until the full maintenance dose of 2 to 3 grains daily is reached During the summer months the maintenance dose should be slightly reduced

WENDT (Munich) has studied the relation of myxoedema and cretinism to carotene and vitamin A In myxoedema the transforma tion of carotene into vitamin A is disturbed In patients with cretinism the vitamin A values of the serum are considerably reduced and it appears that this reduction is essentially a result of the trans formation disturbance of carotene into the vitamin but in cretinism a lack of capacity to store vitamin A seems also to play a part In another communication Wendt reports the successful treatment of three cases of Graves s disease (hyperthyroidism) by means of vitamin A

Goitre —A goitre is an enlargement or hypertrophy of the thyroid gland It may be simple or non toxic or it may be toxic malignant or inflammatory *Simple* or *non toxic goitre* is thyroid enlarge ment without thyrotoxaemia *Endemic goitre* is a simple goitre constantly seen in certain regions of the world probably dependent on a deficiency of iodine in water, air or food *Physiological goitre* is a simple thyroid enlargement of compensatory nature, due to demands made upon the gland by conditions elsewhere in the body *Congenital goitre* is a thyroid enlargement present in the infant at birth and usually due to heredity

MARINE (New York) explains the formation of goitre thus Whenever the thyroid becomes unable to supply sufficient secretion, whether from reduced iodine intake, from increased demands, or following partial thyroidectomy, compensatory hypertrophy occurs This hypertrophy appears always to be the result of direct stimulation by the thyrotropic hormone This is characterized principally by a decrease in the stainable colloid and in the iodine content, by an increase in the blood supply and by a change in the follicular epithelium

The chief factors in the aetiology of endemic goitre are high calcium and low iodine intake, from the water supply or from the diet The part played by iodine deficiency is intelligible, but the role of calcium is not fully understood Vitamin deficiency seems to be a contributory factor, and it is known that certain foods are goitrogenic The thyrotropic hormone of the pituitary must also be considered Districts in which the water supply is deficient in iodine are known to be goitrous, though an exception has been found in New Zealand where the incidence of goitre seems to bear no relationship to the intake of iodine (see PRESCRIBER, 1935, May, 140) In goitrous districts it has been customary to add small quantities of iodine to the water or to the food with a view to its prevention

A survey of the incidence of goitre among school children in Saskatoon, Canada, is reported by BINNING From an examination of 5808 children, 718 cases of goitre were found, two-thirds of which were in girls between 9 and 15 years of age Racial origin seemed to be the factor of greatest importance in the incidence of goitre This was not due to the diet or water supply, because at least half of the races in whom goitre was most frequent were on the same diet as those of British origin Incidence was highest in children belonging to the lower social classes

A useful publication on the subject of goitre is *Proceedings of the Second International Conference on Goitre*, recently published by Huber, Berne, at 25 Swiss francs In this is collected evidence from all parts of the world on the varieties of thyroid disease, their incidence, causes, and treatment, the book forming a symposium of much interest and value

Hyperthyroidism or Thyrotoxicosis —The term hyperthyroidism is applied to all conditions in which evidence exists of overaction of the thyroid, the signs usually being tachycardia, nervousness, loss of weight, tremor, etc Three main forms of hyperthyroidism are recognized (1) Graves's disease or primary thyrotoxicosis, (2) secondary toxic adenoma; (3) thyrotoxicosis of puberty Graves's disease is commonest between the ages of 20 and 30, toxic adenoma usually occurs at the menopause or after Women are more subject than men

Graves's Disease —This disease is known by many names, but 'Graves's disease' seems to be the most appropriate In Germany it is called 'Basedow's disease,' and in Italy it is 'Flajani's disease'

'Exophthalmic goitre' is commonly used, but it must be remembered that both goitre and exophthalmos are quite frequently absent, 'hyperthyroidism' is misleading, as thyroid hyperfunction is only an incidental factor, 'toxic goitre' and 'thyrotoxicosis' are open to similar objections

The pathology of Graves's disease is still under discussion, and it is not definitely known whether the primary lesion is in the nervous system or in the thyroid gland The principal symptoms of a typical case are protrusion of the eyeballs (exophthalmos), tachycardia, and increase in the size of the thyroid gland with raised basal metabolic rate, but many other manifestations are present, and exophthalmos and thyroid enlargement are sometimes absent

The medical treatment of hyperthyroidism has recently been dealt with by several workers, including CLOAKE (Birmingham), FRASER (London), HORDER (London), and NOBLE (Bristol) all these writers cover much the same ground Medical treatment involves several months complete physical and mental rest, preferably in bed this will be beneficial in proportion to the removal of physical and emotional strain Removal of septic foci is essential, and treatment with iodine is beneficial Treatment by x-rays effects improvement, but it must be stopped in time otherwise myxoedema—the other extreme—may follow In severe cases surgical treatment, preceded by a course of iodine (Lugol's solution), is effective A few cases relapse after operation in these a second operation is usually successful For further literature on the surgical aspects of hyperthyroidism readers are referred to recent articles by DUNHILL and by KEYNES, particulars of which will be found in the References at the end of this section

Mention has been made of Lugol's solution This is Liquor Iodi Aquosus, B P C 1934, and contains iodine, 5, and potassium iodide, 7 5, in 100 parts of distilled water, the dose being 5 to 10 minims (0 3 to 0 6 ml) It is regarded as the best form in which to administer iodine in hyperthyroidism An iodine compound, diiodotyrosine, has also been used this will be fully described under Thyroid Therapy It exists along with thyroxine in the gland and is believed to be the precursor of the hormone It has no specific action except that of its iodine content GOTTA (Buenos Aires) reports treatment of twenty five cases using both preparations Twelve received diiodotyrosine alone, seven received Lugol's solution first and diiodotyrosine afterwards, and six received diiodotyrosine first and Lugol's solution later No difference in effect could be noted, the results being identical in all cases

ZARDAY and WEINER (Budapest) have observed that patients with hyperthyroidism require larger doses of barbiturates to be effective An antagonism appears to exist between the thyroid hormone and barbituric acid, which does not include other soporifics

Ovarian Goitre—SANDERS (Memphis, Tenn) reports a case of ovarian struma in a married woman aged 51 A small nodular thyroid goitre was present On operation to remove the ovarian

tumour, this was found to be composed of thyroid tissue Sanders believes that this was a true ovarian goitre, teratomatous in origin, and belonging to that group of cases where the predominant thyroid tissue outgrew the other elements Such cases are rare, but their possibility should be borne in mind

Thyroid Therapy —The position of thyroid substance as a therapeutic agent has been much simplified in the 1932 Pharmacopoeia, where it is now known as *Thyroideum*, thyroid , its synonyms are thyroideum siccum (its 1914 name), dry thyroid, thyroid extract, and thyroid gland It is standardized to contain 0 1 per cent of 'iodine in combination as thyroxine' The dose is 0 03 to 0 3 gm (½ to 5 grains) Thyroid is *no longer to be prescribed in terms of fresh gland* the only form available for prescription is the official dry thyroid in the doses mentioned 'Thyroid extract' is a misnomer, dry thyroid is not an extract

Commenting on the B.P standard of thyroxine iodine in this place three years ago (PRESCRIBER, 1933, May, 161) we offered the opinion that as thyroxine does not represent the entire iodine of the gland, it would have been better to adhere to the total iodine standard until more was known of the part played by the other iodine compound or compounds In the U S P 1936 thyroid is standardized to contain 0 17 to 0 23 per cent of iodine in *thyroid combination*, that is, not necessarily as thyroxine only It has recently been explained by HARINGTON that the B P standard was based on the assumption that the iodine other than thyroxine was inert this view is no longer maintained and it has been shown that the activity of any given preparation of thyroid is determined by its total iodine content The U S.P method is therefore fundamentally correct

The use of thyroid as a remedy is now well established and its indications are generally known Its principal applications are hypothyroidism in its various manifestations, lowered metabolism, obesity (with caution), pregnancy with low B M R , and certain skin diseases MEANS (Boston) utters a warning against the exhibition of morphine in myxoedema, as in this condition tolerance to the drug is greatly lowered A single ¼ grain dose may put a myxoedematous patient into a deep lethargy which might conceivably be fatal

Dealing with thyroid therapy, HOSKINS (Boston) emphasizes the necessity of beginning treatment with small doses, ¼ grain daily at most If the patient has a very low titre of circulating thyroxine, even this dosage may evoke a reaction—nervous tension, tremors, and lachrymation Such a reaction clearly indicates thyroid deficiency and calls for continuance of the treatment after a few days' rest thyroid should be resumed in $\frac{1}{10}$ grain daily doses, from which it may be gradually increased Hoskins remarks also that despite the objections that have been raised to pluriglandular therapy, there is sound basis for the addition of thyroid to a variety of other glandular products when supplementary glandular stimulation is desired in addition to mere substitution therapy

The value of thyroid in the treatment of slowly healing fractures is reported by KONIG (Leipzig) He found when fractures took a long time to heal the B M R was usually below normal In such cases he has given large doses of thyroid in the form of 'elityran' (Bayer), and he noticed that with the rise in B M R the fracture always healed rapidly

PATTERSON (Ruthin Castle, N Wales), whose remarks on thyroid addiction were quoted last year (PRESCRIBER, 1935, May, 146) again refers to the subject It is doubtful, he says, whether thyroid therapy is ever indicated in conditions other than hypothyroidism—even obesity may not call for it He strongly condemns its indiscriminate use for weight reduction and says that self dosing by the laity may be extremely dangerous

BRAIN (London) reports a case in which exophthalmos followed the administration of thyroid Such a sequel, he says, is rare, and is not the direct result of the action of the thyroid hormone, but is due to some other substance which in certain individuals is produced in response to thyroid therapy He suggests that this may be the thyrotropic hormone of the pituitary, which has been found experimentally to produce exophthalmos in animals In normal persons administration of thyroid does not produce exophthalmos but this condition can be brought about experimentally by the administration of drugs which stimulate the sympathetic nervous system, and thyroxine seems to facilitate the action of such drugs

Thyroxine—The crystalline principle of the thyroid gland was first isolated in 1914 by Kendall at the Mayo Clinic It contains 65 per cent of iodine and possesses the physiological action of the gland In 1927 Harington and Barger established the chemical composition of thyroxine and elaborated a process for its synthetic production Synthetic thyroxine is identical in every respect with the natural product, it is not the subject of any patient and it can be produced at a very moderate cost

Thyroxine natural or synthetic is official in the U S P 1936 The average dose is 0 5 mg ($\frac{1}{120}$ grain) The monosodium salt of thyroxine is official in the B P 1932 under the name of thyroxine-sodium It is a white crystalline powder, sparingly soluble in water but more soluble in alkalis, forming unstable solutions It contains 61 to 65 per cent of iodine, and the natural and synthetic products are equally recognized The dose is 0 1 to 1 0 mg ($\frac{1}{1200}$ to $\frac{1}{120}$ grain) When thyroxine is prescribed thyroxine-sodium may be dispensed Thyroxine-sodium is specially suitable for injection, a freshly prepared alkaline solution being used

It is generally recognized that thyroxine is the active hormone of the gland Administered intravenously or subcutaneously its effect is the same as that of thyroid, that is it raises the B M R and relieves the symptoms of myxoedema When given by the mouth, however, its therapeutic effect is considerably less than that of thyroid itself—a discrepancy which has given rise to considerable research

The idea that thyroxine may be destroyed or rendered less active by gastric ferments is untenable, seeing that thyroid itself is fully active by way of the stomach Pure thyroxine is very insoluble and may be difficult of absorption by the stomach or intestine the monosodium salt (thyroxine sodium) is less so, and its introduction into the Pharmacopoeia indicates that it is regarded as an improvement

Although thyroxine contains 65 per cent of iodine, it does not represent the entire iodine content of the gland another organic iodine compound, diiodotyrosine, exists side by side with it Diiodotyrosine is physiologically inert—that is, it does not possess the action of thyroxine or of thyroid, though as already shown it has the action of iodine It has been suggested that diiodotyrosine may be an intermediate stage in the formation of thyroxine from the amino-acid tyrosine, but so far it has not been found possible to confirm this by the synthesis of thyroxine from either tyrosine or diiodotyrosine It has recently been shown that diiodotyrosine and thyroxine between them account for the whole of the iodine in the gland For a time it was thought that diiodotyrosine made no contribution to the active secretion, but recent work shows that it probably does Thyroxine represents the actual activity of the thyroid qualitatively but not quantitatively The diiodotyrosine fraction is inert when separated but appears to play some part when in the gland HARINGTON suggests that the molecule of the complete active secretion contains both thyroxine and diiodotyrosine and that some linkage between the two is ruptured during the hydrolysis necessary for the isolation of thyroxine, the residual activity being confined to the more specific constituent thyroxine

It has been suggested that thyroxine exists in the gland in peptide combination So far it has not been possible to prepare a soluble organic compound of thyroxine suitable for administration, but a substance closely related to it appears to have all the physiological properties of thyroxine with the advantage of being soluble and easily absorbed This is 3 5 diiodothyronine it is easily obtainable synthetically, being the penultimate product in the preparation of synthetic thyroxine It is much weaker than thyroxine, about 50 mg being required to give the effect of 1 mg of thyroxine Successful clinical trials with this compound have been recorded Another substance—a ketonic acid analogous with thyroxine—has been synthesized by CANZANELLI, GUILD, and HARINGTON and shown to possess the characteristic physiological activity of thyroxine in lower degree, the ratio of the activities of thyroxine and of the keto acid being 11 3

While for reasons stated thyroxine has not completely replaced thyroid substance in practice, it has found application in certain conditions Its use in ophthalmology was mentioned in last year's review A recent application is in the treatment of deafness GRAY (London) uses local applications of thyroxine in the treatment of otosclerotic and similar types of deafness Arguing that otosclerosis

is the result of a defective vasomotor response in the small blood vessels of the ear, he thought that thyroxine locally might overcome this defect Fourteen cases were treated, with very considerable improvement in seven, tinnitus being relieved where it was present The method is not suitable in very advanced cases or where serious loss of bone conduction exists or high notes cannot be heard Thyroxine, $\frac{1}{200}$ to $\frac{1}{60}$ grain (0 5 to 1 0 mg) finely powdered and suspended in 4 minims of distilled water, is injected through the tympanic membrane into the inner middle ear by means of a hypodermic syringe A cork is placed between the patient s jaws to prevent swallowing, which would permit the fluid to escape down the eustachian tube The operation is performed once a week No evidence of hyperthyroidism was observed in any of the patients Full details of the procedure will be found in the original article

Antithyroid Hormone —About twenty years ago Moebius introduced a preparation called antithyroidin,' consisting of the serum of thyroidectomized rams for use in the treatment of Graves s disease, his hypothesis being that the blood of such animals contained a substance capable of counteracting thyroid overactivity Some success appears to have attended this treatment, but the method fell into disuse

Three years ago Blum (Frankfort on Main) made an announcement which seemed to confirm the soundness of Moebius's ideas He stated that he had found certain substances in the blood which act as restraining factors on the hormones these he called ' katechins,' from κατεχω I restrain (The term is unfortunate, as catechin is already known as the crystalline principle existing in catechu) Blum claims to have isolated the antithyroid katechin from the blood protein with which it exists in loose combination—he calls it *Tyronorman* Injection of this substance into animals completely neutralizes the rise in B M R caused by administration of thyroid Tyronorman is supplied in tablet form each tablet containing ten ' Blum units,' a unit being equal to 0 001 mg of iodine in combination with thyroid proteins The dose is 6 to 9 tablets daily

Thyroidectomy for Heart Failure —One of the most recent developments in connexion with thyroid treatment is the surgical removal of the gland in cases of angina pectoris and heart failure The work of BLUMGART, BERLIN and others (Boston) has shown that removal of the entire normal thyroid gland even where there is no hyperthyroidism effects wonderful improvement in such cases The result appears to be due to the reduction of B M R the patient being left in a permanent hypothyroid condition The operation requires care as the parathyroids must not be interfered with and the laryngeal nerves must not be injured Seventy five patients were operated on, and the operative mortality was 8 per cent In a more recent communication, BERLIN summarizes the experience of this treatment during two and a half years Seventy per cent of his patients have

been improved by the operation, technical details of which are given. In the last sixty-two patients the operative mortality was *nil*; this is attributed to increased experience in management, improvement in technique, and the use of local analgesia The necessity for extreme care in the operation is again emphasized

Many other workers have reported their experience with this operation BANKOFF (London) reports twenty cases, five of which are described in detail. All patients have shown considerable improvement and have maintained this for periods varying from three months to a year No fatality is recorded BRENNER (Birmingham) deals with the subject in considerable detail and reports seven cases with encouraging results and no fatality. HEPBURN (Toronto) reports five cases Patients with angina pectoris showed much improvement, but those with persistent cardiac failure showed little benefit PRATT (New York) suggests extension of the method to the treatment of arteriosclerosis, syphilis, and renal disease, and reports results in nineteen cases He stresses the potential dangers of the operation.

A general survey of the literature seems to show that the operation has great possibilities, but that its application should be restricted to carefully selected patients and its performance to surgeons of great skill and experience, also that the possible dangers of the operation should be kept carefully in mind

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THE PARATHYROID GLANDS.

THOUGH closely related anatomically to the thyroid, the parathyroid glands are independent of it in development and function. They are minute kidney-shaped bodies, usually four in number, situated on the posterior borders of the lateral lobes of the thyroid. They are made up of three types of cells: the *principal cells* and the large and small *oxyphilic cells* which appear to be derived from the principal cells as they do not appear until about the tenth year. The parathyroids contain no iodine, or only a negligible amount, and their function appears to be in some way connected with calcium-phosphorus metabolism.

The upper parathyroids were first described in 1880; the lower pair in 1895. It was then found that the symptoms of tetany which frequently followed removal of the thyroid were actually due to removal of portions of the parathyroids at the same time. When these were left carefully in situ, removal of the thyroid was not followed by such symptoms.

Further experimental work on the parathyroids has since brought to light much regarding their function; still the exact part played by them has not been definitely determined. Many workers have advanced hypotheses to explain why injury to the parathyroids produced tetany. At first it was thought that the symptoms were due to guanidine intoxication, which the parathyroid secretion neutralized. This hypothesis has not been confirmed, but it is believed that the parathyroids are essential for the combination of phosphoric acid with creatine, and that a by-product of this action is methylguanidine; it is possible therefore that parathyroid dysfunction may result in an excess of methylguanidine, which is toxic.

The hypothesis that parathyroid tetany is due to accumulation of guanidine in the blood is negatived by SAUNDERS (Univ. of Durham), who failed experimentally to find any guanidine in the blood of parathyroidectomized animals. Further, injected guanidine was removed as quickly from the blood of animals in tetany as from that of normal animals; it appears improbable therefore that the parathyroids regulate either the production or the destruction of guanidine.

It is known that the ionic or dialysable calcium in the blood-serum controls the irritability of the nerves and muscles: shortage of this element thus induces tetany. When Collip succeeded in preparing an active extract of parathyroid, injection of which restored blood-calcium and relieved tetany, the relation of the parathyroids to blood-calcium became established. As the ratio of calcium to phosphorus is an important factor and the two elements are closely interrelated in metabolism, it is assumed that the parathyroids exercise some control over phosphorus also.

The normal amount of calcium in the blood-serum of man is

from 9 to 11 mg per 100 c cm , or 0 009 to 0 011 per cent that of inorganic phosphorus averages 2 5 to 4 mg per 100 c cm The parathyroids do not metabolize calcium from the food They simply mobilize the calcium in the blood by withdrawing it from other parts of the body, chiefly the bones Consequently in cases of overactivity of the parathyroids the bones are deprived of much of their calcium and become fragile Realization of these conditions has led to one of the most interesting of recent developments—the possible relation of vitamin D to parathyroid function Some years ago it was shown that vitamin D in the form of irradiated ergosterol had the effect of raising the serum calcium level and relieving symptoms of parathyroid deficiency, but the exact nature of this action has not been explained Whereas parathyroid extract takes effect in a few hours vitamin D requires days to produce the same result and therefore is useless in an emergency

A relationship appears to exist between the parathyroids and the gonads It has been noticed that parathyroid tetany very rarely appears in men while in women such attacks are closely associated with the menstrual cycle McCULLAGH and KEARNS (Cleveland Ohio) have studied the subject and conclude that the sex glands have a pronounced effect on the neuromuscular excitability in human parathyroid tetany Variation in amount of sex hormones in the body was not correlated with alterations in the levels of serum calcium and phosphorus and it appears probable that their effect is produced through a separate mechanism

A functional synergism between the parathyroids and the pancreas is suggested by FERRANNINI (Italy) who has studied the action of parathyroid extract on the glycaemic curve and on the glycosuria of patients in different stages of diabetes In normal subjects parathyroid extract lowers the glycaemia during fasting and increases carbohydrate tolerance its action being very similar to that of insulin The parathyroids and the pancreas form part of the sympathetic group of glands and Ferrannini thinks that parathyroid extract acts by way of the parasympathetic system

From time to time reports come to hand of the presence of parathyroid tissue in the thymus Such cases though fairly frequent in animals are rare in man In last year s review (PRESCRIBER 1935 May, 152) four cases were mentioned—two in adults and two in infants In the adult cases both principal and oxyphilic cells were present , in the infants no oxyphilic cells were found In all cases the discovery was made *post mortem* and the glands found in the thymus were aberrant, that is they were missing from their usual situation on the thyroid

A disturbance of the normal function of the parathyroids has been observed during pregnancy The maternal serum calcium decreases in the later months and increases again during the early puerperium This is due probably to the demands for calcium made by the growing foetus

Parathyroid Disorders.—As with the thyroid, the two main disturbances to which the parathyroids are subject are under- and over-function. Hypoparathyroidism, which usually follows upon a subtotal thyroidectomy in which the parathyroids have been injured, produces a state of chronic tetany, with low serum-calcium, high serum-phosphorus, excitability of the neuro-muscular system, and a tendency to the development of cataract. Hyperparathyroidism, or excessive function, shows itself in generalized osteitis fibrosa with high serum-calcium, low serum-phosphorus, a tendency to under-excitability of the neuro-muscular system, rarefaction and softening of the bones, and fractures.

Hypoparathyroidism.—Parathyroid tetany may be either post-operative, following upon removal of or injury to the parathyroids, or it may be spontaneous; the spontaneous form is rare. Post-operative tetany appears in from one to four days after operation. The patient feels a tingling in the arms and hands on the second or third day. This becomes more intense and after a few weeks he passes into the stage of chronic tetany, in which paraesthesia is the most constant symptom. The serum-calcium is low—usually 5-6 mg. per 100 c.cm.—and the serum-phosphorus is high—5 mg. or more per 100 c.cm. The severity of the symptoms does not depend on the lowness of the calcium level: probably it varies inversely with the ionic calcium, which there is no means of measuring. When the serum-calcium rises above 8 mg. the symptoms become mild and disappear. Treatment consists in administration of calcium: slow intravenous injections of 10 c.cm. of 5-10 per cent. calcium chloride solution will afford immediate relief, and a high calcium diet will help to maintain this. Should spasms recur in spite of treatment, injections of parathyroid extract (20 to 40 units daily) are helpful, but its action is too slow for use in emergency. A diet rich in calcium—milk, eggs, and green vegetables—should be given, with calcium chloride, lactate, or gluconate, by mouth. An adequate amount of vitamin D should be given in the diet or in the form of irradiated ergosterol or calciferol.

HERLIHY (Lewisham) reports a case of the spontaneous type in an unmarried woman aged 25, following on an attack of influenza. The blood-calcium was 7·3 mg. Pain in the renal region and pus in the urine called for suitable treatment. Calcium gluconate and parathyroid extract relieved the symptoms of tetany, and vitamin D was given in large doses. The patient recovered.

STACEY (London) reports three cases of low-calcium tetany, two postoperative and one a sequel to influenza. The serum-calcium at the start was respectively 7, 6·7, and 5·1 mg., and the inorganic phosphorus 5·1, 5·7, and 8·0. In all three cases administration of calciferol (crystalline vitamin D) in large doses was followed by rapid relief with rise in calcium and lowering of phosphorus. A diet containing adequate calcium was given in order to provide for absorption and to minimize the risk of decalcification.

Calcium gluconate and extra milk provided this, and the patients have been maintained free from symptoms and with normal blood findings

The question of tetany in the newborn is discussed by HELLMAN and ROTHSTEIN (New York) Two cases of low-calcium tetany have recently been observed by them, the symptoms were unmistakable and the blood calcium was 7 4 and 7 5 mg Treatment with vitamin D, ultraviolet irradiation, and calcium gluconate was effective in restoring the infants to normal health Low calcium tetany in the newborn, they say, is increasing in frequency and is apt to be overlooked or wrongly diagnosed

'A T 10'—A preparation called 'A T 10' was introduced about two years ago by Holtz (Berlin) for the treatment of parathyroid tetany It is described as an oil soluble fraction of irradiated ergosterol which does not contain vitamin D but which has a specific influence on the blood calcium It is given orally, and its effect, though slower than that of parathyroid, is said to be more lasting The initial dose is 5 to 10 c cm daily for three days, then 1 to 2 c cm daily for ten to fourteen days after which 1 to 2 c cm three times a week is sufficient The serum calcium rises considerably after two or three days but the results must be carefully watched as its action is cumulative

In last year's review (PRESCRIBER 1935, May, 154) several reports from continental literature were abstracted, all of which were favourable to the use of 'A T 10 at the same time emphasizing certain precautions as to dosage etc More recently ELLIOTT (London) reported a case of parathyroid tetany in a boy aged 13, the serum calcium being 5 mg and the phosphorus 8 9 mg, with a B M R of minus 26 per cent Parathyroid extract effected only moderate improvement Then A T 10 was given orally in doses of 5 c cm on alternate days The serum calcium rose slowly but steadily and the symptoms of tetany disappeared at a level of 7 8 mg calcium The calcium rose further to 9 3, but fell again to 8 2 when 'A T 10' was discontinued Large doses of calciferol were then given the calcium rose steadily to 12 2 and the phosphorus dropped to 3 7 mg Eventually this was stopped and the patient remained normal It appears from this that calciferol has the same effect as 'A T 10' and is more permanent in its results

Hyperparathyroidism—It is now recognized that overfunction of the parathyroids gives rise to generalized osteitis fibrosa This is a chronic condition characterized by rarefaction and softening of the bones, deformity of the skeleton, cystic degeneration, and fractures Though the condition was first described by von Recklinghausen in 1891, it is only within the last decade that the responsibility of the parathyroids has been recognized Hyperparathyroidism is the result of hyperplasia of the glands caused by a tumour The serum calcium is high and the serum-phosphorus low The superactivity of the glands causes withdrawal of calcium from the bones, with the

results already described Treatment consists in surgical removal of the parathyroid adenoma, which relieves the symptoms and restores the calcium metabolism to normal

WILDER and HOWELL (Mayo Clinic) review 135 cases occurring in their own clinic and reported in the literature They point out that to establish the case as one of true hyperparathyroidism it is essential that the skeletal abnormality should be that of generalized osteitis fibrosa, that the blood-calcium should be high, and that a tumorous enlargement of the parathyroids should exist Incidence seems to be highest in industrial districts such as those of England and the northern States of the U S.A where the atmosphere is smoky, Italy, Spain, and the southern United States have a clearer atmosphere and show a lower incidence This is attributed to the ultraviolet rays of the sun, which produce vitamin D in the body Lack of vitamin D can be sustained by most adult persons without harm it is the few in whom the cells of the parathyroids possess a special capacity for proliferation into tumours who contract the disease through lack of sunshine The proportion of females to males affected is about three to one It is pointed out further that operative removal of the tumour is almost always followed by tetany, which must be treated appropriately

In a lengthy article dealing largely with surgical technique, LAHEY and HAGGART (Boston) remark on the frequent failure to detect a parathyroid adenoma One reason is the not infrequent atypical position of the parathyroids An adenoma of a parathyroid usually converts that structure into a globular mass and changes its colour to a pale white rather than the brownish colour characteristic of a normal gland Should this not be found a careful search must be made in the thyroid and nearby structures, and should the adenoma still not be detected one of the parathyroids should be removed and submitted to a pathologist for microscopic examination

Discussing the pathology of osteitis fibrosa, TAYLOR (London) points out that there is no concentration of calcium in the body, and deprivation of it results in a constant drain from the skeleton into the urine and faeces The absorption of calcium may be hindered by excess of phosphates or carbonates in the diet, or by incomplete digestion or absorption of fats, which causes the precipitation of calcium soaps in the intestine, or by lack of vitamin D, or possibly by incomplete protein absorption from the gut The excretion of calcium is also influenced by variations in the metabolism of other substances, the effects of which are reflected in the calcium content of the serum He points out that bones undergoing prolonged decalcification, as in osteitis fibrosa, are on the one hand under the influence of the decalcifying agent and on the other under that of the response of the weakened bone whereby the osteoblasts are stimulated to form new bone by an increased output of phosphatase, which, however, is constantly being swept away into

the circulation, causing a high concentration of the phosphatase in the plasma Taylor definitely considers that the hypercalcaemia is due to hyperparathyroidism and to no other cause The low serum phosphorus is an effect of ionic dissociation and is not specific to the parathyroid hormone

Some years ago (PRESCRIBER, 1931, May, 182) mention was made of an advanced case of hyperparathyroidism reported by Quick and Hunsberger, of Philadelphia Removal of a parathyroid tumour arrested the disease, but the deformities that had occurred left the patient a hopeless cripple A subsequent report of the same case has now been given by QUICK, HUNSBERGER, ELIASON, and HUDSON, who show that after removal of three tumours at different times and surgical treatment of his deformities the patient's legs have been straightened and he is now able to go about on crutches The disease appears to have been permanently arrested, and the only unfortunate feature is that surgical interference was not done earlier The case emphasizes the need for complete removal of the tumours and the advisability of a second exploratory examination if signs of hyperparathyroidism persist

BORG (St Paul, Minn) shows where the dentist can co-operate with the physician or surgeon in the detection of hyperparathyroidism Most of such cases begin with signs which lead the patient to seek dental advice Decalcification of the jaws is an early sign, and the bony resorption about the roots of the teeth causes loosening and favours development of pyorrhoea With a better knowledge of the possible significance of these signs the dentist can spare the patient much needless dental interference and unnecessary loss of teeth by suspecting hyperparathyroidism and sending the patient for proper treatment

ALBRIGHT and BLOOMBERG (Boston) review twenty three cases of hyperparathyroidism associated with renal disease, and point out that renal disease occurs more commonly than bone disease Finely granular casts are frequently found in the urinary sediment The granules contain calcium—probably calcium phosphate Their continuous presence indicates that intrarenal drainage is in progress Probably the factors governing the formation of these casts are the same as those governing stone formation in hyperparathyroidism, namely, concentration in the urine of calcium, phosphates, and hydrogen ions

LERICHE, JUNG, and SUREYYA (Paris) hold that scleroderma originates in overfunction of the parathyroids In a further communication, LERICHE and JUNG show that scleroderma is a manifestation of an abnormal calcium content of the skin following osteolysis due to hyperparathyroidism The involved skin has been found to contain from 20 to 30 per cent more calcium than normal skin and the fat in adjacent regions has almost double the normal calcium content The initiating factor is the parathyroid osteolysis follows and cutaneous atrophy is the result

Parathyroid Therapy.—The British Pharmacopoeia, 1932, contains no preparation of parathyroid. The new United States Pharmacopoeia (1936) contains Liquor Parathyroidei, solution of parathyroid or parathyroid extract. It contains the water-soluble principle or principles of the glands of 'healthy domesticated animals used for food by man.' One c.cm. has a potency of 80 to 120 units, a unit representing one-hundredth of the amount required to raise the calcium level of 100 c.cm. of the blood-serum of normal dogs *one milligram* in 16-18 hours. The average dose is 25 units hypodermically.

The British Pharmaceutical Codex (1934) contains Extractum Parathyroidei (synonym, 'parathormone'), one unit of which is one-hundredth part of the amount required to raise the blood-calcium of a dog by *five milligrams* per 100 c.cm. The dose is 20 to 40 units. This is the old potency: it has recently been reduced to one-fifth of the old standard, and the U.S.P. represents the standard now in force. The concentration of the extract and the volume of the injections remain the same.

AUB (Boston), discussing the clinical use of the new extract, says that the effect of parathyroid extract is greater when it is needed. Thus, 75 units a day (new standard) may be enough to raise the blood-calcium from 4·5 to 7 mg. per 100 c.cm. in a case of low-calcium tetany, but in normal persons it may require 500 units a day to raise the level from 10 to 12 mg. Individuals vary greatly in susceptibility, and the dosage must be regulated by determinations of the blood-calcium every few days. Hypercalcaemia gives few clinical indications until a level of 12 mg. is reached, when loss of appetite, nausea, and fatigue appear. Repeated doses are more effective than a single injection The effect of parathyroid extract does not appear until about four hours after injection; it lasts for twenty hours. Calcium gluconate, on the other hand, shows its effect immediately and lasts about two hours. Vitamin D, in large doses, gradually elevates the blood-calcium over a period of days, and its effect is maintained for at least two weeks after therapy is discontinued; an overdose, therefore, causes signs of hypercalcaemia over a long period. A serious drawback to parathyroid extract is a gradual loss of its effect: an apparent immunity is established. Its chief use is in the treatment of low-calcium tetany, in which it may be a life-saving measure. It is of use also in conditions in which decalcification of the body is desired, such as abnormal deposits of calcium in the tissues and abnormal storage of metals (lead or radium) in the bone.

Infection appears to play a part in the success or failure of parathyroid extract in raising the blood-calcium and relieving symptoms of tetany. LINDER (Univ. of Capetown) has shown that typhoid fever decreases its action and that pulmonary tuberculosis increases it.

Reference was made last year (PRESCRIBER, 1935, May, 157) to

the work of GOADBY and STACEY (London) who showed that the first apparent action of parathyroid extract in normal persons is to increase the rate of excretion of phosphorus in the urine and that this increased excretion of phosphorus is independent of the concentration of inorganic phosphorus in the blood plasma Further studies by the same workers confirm these findings and show that parathyroid extract acts directly on the kidneys to produce a phosphate diuresis this action being independent of its effect on the blood calcium In persons in whom the excreting power of the kidneys is grossly impaired parathyroid extract fails to cause the same increased excretion of phosphorus in the urine as occurs in normal persons

Parathyroid therapy with calcium has been shown by HASKELL and CANTAROW (Philadelphia) to be of service in the treatment of ulcerative colitis A number of patients were so treated and showed complete recovery or great improvement in the majority of cases This is believed to be due to the influence of calcium on tissue nutrition

Prior to the introduction by Collip of the extract containing the active hormone preparations of the dried gland were employed empirically in various conditions tablets of dried parathyroid substance being given orally in doses ranging from $\frac{1}{60}$ to $\frac{1}{10}$ grain but little if any evidence has been adduced to show that benefit from their use was due to the parathyroid substance The only physiological effect obtainable from the administration of parathyroid is a rise in the serum calcium level and the rational way to achieve this is by the administration of the extract in definite dosage

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THE ADRENALS.

UNDER the name of suprarenal capsules the adrenal glands have been known to anatomists for a long time In 1849 Addison demonstrated that the disease which now bears his name was associated with certain destructive lesions of the adrenals In 1894 Schafer and Oliver showed that extracts of the adrenal medulla had the property of raising the blood-pressure In 1901 Takamine and Aldrich independently discovered the active principle of the medulla, adrenaline Recent research on the adrenal cortex has brought to light other interesting points connected with the nature and function of these glands

The adrenals are two small flattened bodies of a yellowish colour, situated one on the upper end of each kidney, hence their name Each weighs about 4 gm and consists of two portions, a cortex and a medulla, the whole surrounded by a fibrous capsule The cortex consists of a fine connective tissue network in which is embedded the glandular epithelium The medulla is composed of finely granular chromophilic cells permeated by large venous sinusoids The granular cells stain green with ferric chloride (the reaction of adrenaline) and brown with chromic acid Control of the two tissues appears to be independent, that of the cortex being humoral, that of the medulla nervous

The cortex and medulla contain separate hormones that of the medulla is the well-known adrenaline, while the hormone of the cortex is still under investigation As these hormones discharge separate functions, it will be necessary to consider the adrenals under the heads of their component parts, the medulla and the cortex, but before doing so it is desirable to discuss some aspects of the glands as a whole

The operation of partial adrenalectomy or of denervation of the

adrenals as a therapeutic measure in some conditions such as diabetes has had a certain vogue The evidence implicating the adrenals in such cases is very meagre, moreover, the operation has been followed by serious results ROGOFF (Chicago) reports a case in which Addison's disease followed adrenal denervation for diabetes mellitus, and he points out that surgical interference with the adrenals in the absence of actual tumour is to be strongly deprecated FREUD, LUWISCH, and OESTREICHER report experiments on animals showing that adrenalectomy is followed by ulceration of the stomach and they suggest that gastric ulceration may be due to pituitary adrenal deficiency

The use of whole adrenal substance as a therapeutic agent is unusual, especially now that two separate hormones are recognized having different actions PUSEY and RATTNER (Chicago) report the successful use of whole gland in skin disorders having a menstrual factor A woman who always had a severe facial eruption during her periods—first diagnosed as lupus erythematosus—was treated with tablets of adrenal substance shortly before and during menstruation, and from the institution of this treatment the eruption failed to appear HICKS and MITCHELL (Adelaide) report the treatment of Addison's disease by means of whole gland this will be referred to more fully when dealing with the cortex

The Adrenal Medulla —The function of the medullary portion of the adrenals appears to be concerned mainly or entirely with the secretion of the hormone adrenaline, which circulates in the blood to maintain the blood pressure and to reinforce it in cases of emergency such as fright emotion etc In short, it augments the activity of the sympathetic nervous system in times of stress The medulla is not essential to life

Adrenaline —While the pressor action of the adrenal medulla was demonstrated by Schafer and Oliver in 1894, it was not until 1901 that the hormone was isolated The chemical constitution of this base was definitely established in 1903, and a year later adrenaline was produced synthetically For a time the synthetic product proved to be less active than that obtained from the glands, but further research resulted in the production of a laevorotatory adrenaline identical chemically and physiologically with the natural substance

The hormone of the medulla is official in the B P 1932 as *Adrenalina*, adrenaline, the U S P (1936) name is 'epinephrine' The formula of adrenaline is $C_9H_{13}O_3N$, and both natural and synthetic are recognized The dose is 0 1 to 0 5 mg ($\frac{1}{600}$ to $\frac{1}{120}$ grain) The official solution, *Liquor Adrenalinae Hydrochloridi*, contains adrenaline, 1 1000 with dilute hydrochloric acid sodium chloride, and chlorbutol The dose, by subcutaneous injection, is 0 12 to 0 5 ml (2 to 8 minims)

In the prescription of adrenaline its incompatibilities must be kept in mind Adrenaline is particularly liable to oxidation, either

by the air or by some oxidizing agent. The acid in the official solution prevents oxidation; alkalis not only neutralize this acid but themselves promote oxidation. Adrenaline should never be prescribed in alkaline or even in neutral solution. Indeed it is safest to prescribe adrenaline solution alone, without any admixture except normal saline solution.

As a vasoconstrictor, adrenaline has now to some extent given place to ephedrine, an alkaloid obtained from *Ephedra* species. The pressor action of ephedrine is very similar to that of adrenaline, but considerably slower. It has the advantage, however, of being more prolonged in its effects, of being safer, and of being active when given by the mouth, which adrenaline is not. Adrenaline still holds the field for use where immediate action is required.

One of these emergency uses to which adrenaline has been put is its injection into the heart in cases of heart-failure. For some time the literature on this subject was extensive, and due reference was made to it in these pages; it has now become a recognized procedure.

Some years ago (PRESCRIBER, 1933, May, 171) reference was made to the findings of Hungarian workers that adrenaline as met with in commerce was not the same as the hormone existing in the gland, but was a decomposition product of the original substance, which they named *novadrenaline*. Other workers again claimed to have shown that a stable substance, resembling adrenaline in all respects except that it was resistant to oxidation, existed in a perfusate of the gland and was probably a precursor of the hormone. HEARD and WELCH (Toronto) have followed up these findings and confirm the existence of a stable sympathomimetic substance in the perfusate of the gland, and that ascorbic acid or vitamin C (contained in the cortex) plays a part in this stabilization.

The Adrenal Cortex.—It is known that the adrenals are essential to life: their complete removal from an experimental animal invariably results in death, and that in a very short time. That death is the result of the absence of the glands has been proved repeatedly. Administration of adrenaline to an adrenalectomized animal, however, will not keep the animal alive; something other than the known hormone must be the essential constituent. Further, the adrenal medulla may be removed without fatal result so long as the cortex is left intact. The cortex, then, is the portion of the gland essential to life.

Physiology.—The exact function of the cortex has yet to be determined. It is known that cortical extract relieves some of the symptoms of Addison's disease; some relationship to the sex glands has also been demonstrated, hyperplasia of the cortex being known to lead to virilism. The presence of vitamin C (ascorbic acid) in the cortex further complicates the matter, and recent work indicates that the cortex has some regulating effect on the sodium balance of the body, just as parathyroid has on the calcium balance.

Cortical Hormone.—The isolation of a crystalline hormone from the adrenal cortex, as reported by Kendall and associates of the Mayo Clinic, was mentioned in last year's review (PRESCRIBER, 1935, May, 162). These workers succeeded in isolating a crystalline substance having a constant composition and containing no adrenaline. Its empirical formula is $C_{20}H_{30}O_5$; it has the properties of a hydroxy-aldehyde and possesses the physiological activity of the cortex in that it keeps adrenalectomized animals in normal condition. It differs from adrenaline in containing no nitrogen.

In a more recent communication KENDALL states that this crystalline material appears to consist of more than one compound. Its fractionation is difficult, but the matter is now under investigation and the result will be reported as soon as this has been accomplished.

The Cortex and Vitamin C.—The discovery of the presence in the adrenal cortex of vitamin C (ascorbic or cevitamic acid) adds another and a rather puzzling factor to the physiology of the adrenals. The adrenal cortex of the ox has been found to possess an astonishingly high antiscorbutic activity, being more potent in vitamin C than any other natural source hitherto known. The medulla also contains vitamin C, but in somewhat lower concentration. Several hypotheses have been advanced to account for this: the adrenals cannot be regarded as a reserve store for vitamin C, and it has been suggested that the vitamin is essential to the normal functioning of the organ.

TISLOWITZ (Warsaw) has compared the action of adrenal cortex extract with that of vitamin C on animals with adrenal insufficiency. The action of the two substances showed a certain complementary relationship, and he thinks that vitamin C assists the action of the cortical hormone in its relation to the circulatory system.

HOFF (Konigsberg) thinks that the ascorbic acid of the adrenals, or rather its deficiency, is responsible for the characteristic pigmentation of the skin in Addison's disease. A similar pigmentation is often seen in scurvy and points to deficiency or faulty absorption of vitamin C. Treatment with ascorbic acid has been found to remove the pigmentation caused by sunlight.

THADDEA (Berlin) thinks that vitamin C assists the cortical hormone in combating infections, having found that cortical extract acts better in certain cases when combined with vitamin C. He thinks also that the vitamin has something to do with the relationship between the adrenal cortex and the gonads.

The Cortex and Sodium Metabolism.—The part played by sodium in adrenal insufficiency has been studied by LOEB, ATCHLEY, and STAHL (New York). Their results indicate that a definite relationship exists between sodium metabolism and the cortical hormone. When cortical insufficiency develops, the sodium concentration of the blood is decreased because of an increased rate of sodium excretion. The diagnostic change in the sodium level becomes more apparent when salt is withdrawn from the diet. The withdrawal of salt, however, may result in an adrenal crisis dangerous to the patient.

Conversely, the administration of salt will frequently alleviate acute adrenal insufficiency, and the continuation of this therapy mitigates to a considerable extent the signs and symptoms of Addison's disease. Finally, it should be recalled that, when destruction of the adrenal glands is complete, salt alone will not maintain life.

Adrenal Disorders.—As with other glands, disorders of the adrenals may be divided into two groups—under- and over-activity, conditions which may affect either the medulla or the cortex. Underfunction and overfunction of the medulla are both theoretically possible, but underfunction is not clearly understood. A condition has been described as hypoadrenia, but it is doubtful if the adrenals are responsible. Overfunction of the medulla is associated with tumours of that tissue. Underfunction of the cortex results in Addison's disease, while overfunction produces certain sexual abnormalities the nature of which depends on age and sex.

Cortex, Underfunction.—The chief manifestation of underfunction of the adrenal cortex is Addison's disease. The remarkable results obtained by the use of cortical extract in this condition establish the relationship beyond a doubt; at the same time it must be borne in mind that the extract has little or no effect on the underlying condition, such as tuberculosis or syphilis, when this exists. The cortical extract replaces the deficient secretion; it does not remove the cause.

Adrenal Cortex Extract.—Although the crystalline hormone of the adrenal cortex has been isolated, it is not yet available for therapeutic use. Active extracts of the adrenal cortex are available, free from vitamin C and containing not more than traces of adrenaline. The British Pharmaceutical Codex describes such a preparation—*Extractum Suprarenalis Corticis*—standardized by its power to keep adrenalectomized animals alive when one millilitre is injected twice daily. The extract is administered subcutaneously, intramuscularly, or intravenously in cases of Addison's disease. During the acute stage of crisis 10 to 20 c.cm. or more is injected intravenously, together with large doses of normal saline and dextrose to prevent dehydration. Maintenance doses of 5 to 10 c.cm. are given subcutaneously or intramuscularly.

Eucortone and *Eschatin* are proprietary brands of this extract and conform to its standards. The B.P.C. gives 'cortin' as a synonym for the extract, but it might be well to avoid this term as it has been applied by Hartman to a different product as well as having been suggested as the name for the crystalline hormone. The American Medical Association recommends as a non-proprietary name *Adrenal Cortex Extract* (Extractum Adrenali Corticis); a name for the hormone is to be decided later. It may be remarked that 'adrenal' is a better term than the obsolescent word 'suprarenal.' In addition to being shorter and more elegant, it is more accurate; the adrenals are attached *to* the kidney, but are not always *above* it.

Cortical extract of various makes has been used with considerable success in treatment of Addison's disease. In some cases the effects

are dramatic, in others treatment is less satisfactory The disease being usually the result of progressive destruction of the cortex, treatment can only replace the normal secretion and, as in the case of insulin, must often be continued indefinitely When the disease is caused by tuberculosis of the glands, the extract may be serviceable in tiding over the critical period while the disease itself is being treated

KENDALL (Mayo Clinic) points out that when adrenal cortex extract is given alone it does not reduce the blood-urea, but when sodium chloride is given in addition the blood urea is promptly restored to normal A preparation of adrenal cortex may be made which is active in the absence of sodium chloride This does not stimulate the muscles like the other extract, the most active extract is one which combines the effects of both Kendall suggests that the syndrome seen in tumours of the cortex may be due to the production of an abnormal substance rather than to excessive production of the cortical hormone A relationship exists between the adrenal cortex and thyroxine (*see* Thyroid Gland), but whether adrenal cortex extract will be of value in the treatment of hyperthyroidism has not been proved

GROLLMAN, FIROR, and GROLLMAN (Baltimore) describe a simple method for the preparation of an extract suitable for oral administration An acetone extract of the glands is evaporated and treated with animal charcoal, which adsorbs the hormone complex This adsorbate maintains life in adrenalectomized animals and appears to have the same action as cortical extract It is presumed that in the gastro-intestinal tract the hormone is liberated from the charcoal and absorbed into the system

HICKS and MITCHELL (Adelaide) advocate the treatment of Addison's disease with a preparation of whole gland Commercial preparations of whole gland, they say, are without effect The preparation they use is made from fresh adrenal tissue, defatted, minced, and dried rapidly at 37° C (98 6° F) Daily doses of 3 gm (45 grains), given by mouth, are effective in restoring a large measure of health to sufferers from Addison's disease Adrenal cortex extract is first given to bring the patient to the proper condition, after which treatment with whole gland is instituted The sodium chloride intake must be increased to 10-15 gm daily

Treatment by Addison's disease by transplantation of the adrenal cortex has been tried in two cases by BEER and OPPENHEIMER (New York) One patient died, but the other showed considerable improvement The grafted material was obtained from another patient whose kidney had been removed, and the transplantation was made immediately A similar case (unsuccessful) was mentioned in this place two years ago (PRESCRIBER, 1934, May, 171)

Sodium Chloride Treatment—In a recent review (PRESCRIBER, 1934, May, 171) an account was given of the work of Harrop and associates, who showed that the value of cortical extract in Addison's

disease was due mainly to its action in maintaining the Na and Cl ions in the blood The blood of adrenalectomized animals shows a marked decrease in sodium chloride, with increased urinary output of the same salt To maintain the osmotic pressure of the plasma an increased output of water is necessary, with the result that blood concentration follows causing shock and death In cortical in sufficiency (Addison's disease) a high salt intake is necessary, and the use of common salt (sodium chloride) is indicated either as supplementary to cortical extract or in place of it

Since that announcement a number of reports have appeared on the use of common salt in the treatment of Addison's disease, with or without adrenal cortex extract Several of these were mentioned in last year's review SIWE reports that he found it impossible to administer salt by the mouth as it provoked vomiting he cured his case with cortical extract alone, and he thinks that severe adrenal deficiency may exist without a decrease in the blood sodium BLANKENHORN and HAYMAN (Cleveland) record the successful treatment of a patient in crisis with intravenous sodium chloride when cortical extract had apparently failed In the subacute phases of the disease, salt by mouth maintained the patient in relatively good condition, and for seventeen days the daily dose of 12 gm of sodium chloride was replaced by a mixture of sodium sulphate, phosphate, and carbonate containing the same quantity of sodium

At a discussion of the subject held quite recently by the Royal Society of Medicine, GRAHAM described five cases so treated at St Bartholomew's Hospital One patient died, two showed improvement but died later, another had shown remarkable improvement after a single dose Levy Simpson described six cases and concluded that salt by mouth might be of real value in some cases and it might be useless in others Its emetic action was a drawback, but the use of other sodium salts might overcome this difficulty The maximum amount most patients could take was 10 gm daily, but sometimes 20 gm or more was necessary Cortical extract gave better results than salt alone, and when the dose of extract was adequate salt was unnecessary The cortical hormone was known to regulate the balance of sodium chloride and other minerals The hope was expressed by some members that a cheaper cortical extract might be available, and it was remarked that the pure crystalline hormone might eventually be the only treatment

Cortical Extract in Other Conditions—As the exact function of the adrenal cortex is not thoroughly understood, it is not surprising that the use of the extract should be suggested in other conditions which might be attributed to cortical insufficiency, such as asthenias of the nervous, muscular, and circulatory systems, gastro intestinal instability, reduced metabolism and growth, and reduced activity of the sex organs These alterations in function, if not too far advanced, can, it is said, be corrected by the injection of cortical extract

Adrenal cortex extract seems to be of some service in cases of vomiting especially of pregnancy Last year (PRESCRIBER, 1935 May, 166) reference was made to the experience of Kemp (Vancouver) who treated early vomiting of pregnancy by oral administration of dried cortical extract A more recent report by FREEMAN and MELICK (Worcester, Mass) states that injections of cortical extract gave excellent results in a case of vomiting of pregnancy, and these workers are now trying the effect of the extract in other forms of vomiting TORRE BLANCO and RIESGO DEL CAMPO (Madrid) also report a case of severe vomiting and acidosis during pregnancy in which injection of cortical extract countered the excessive lactic acid formation in the blood while the production of acetone bodies was checked by insulin dextrose treatment

WHITEHEAD and FOX (Denver, Col) studied the effect of adrenal cortex extract on the course of infection in animals with diphtheria, botulism, and tetanus toxins No real protective action was afforded in any case , in the case of botulinus toxin a slight protection was afforded against small doses of the toxin

It is held by many that the adrenal cortex plays a part in the *defensive mechanism of the body against infection and that cortical* deficiency reduces that power of resistance On this basis a liquid preparation called *Adsperlen* has been introduced, containing extract of adrenal cortex with spleen and thyroid This, given orally in doses of ten drops thrice daily, is said to combat infections and to raise low blood pressure very rapidly

Cortex Overfunction —It has already been shown that over function of the adrenal cortex manifests itself in what is known as the adrenogenital syndrome This syndrome is characterized by the appearance of male sex characters in the female, and is associated with a retrogression of the primary and secondary feminine characters and functions The main changes are (1) distribution of hair according to the male pattern , (2) alterations in bodily contour towards that of the male , (3) immature development of the genitalia under development of the mammae, and disturbances of menstrua tion , (4) a more or less male psychological outlook

In last year's review (PRESCRIBER 1935, May, 167) the work of Broster was mentioned He describes four types of the syndrome *indicating cortical overfunction (1) pseudo hermaphroditism,* showing itself after puberty , (2) virilism in which changes appeared after a normal puberty , (3) mild virilism associated with other endocrine disturbances after puberty—the fat type , (4) post menopausal virilism The effect of unilateral adrenalectomy has been very gratifying in the second group, but not in the first and third In the first group operation after puberty is too late to change characters already fixed In the third group it would appear that the determining factor is a disturbance of the balance between the adrenal and the anterior pituitary The condition appears to have its origin *in utero* it is not a disease but is a definite deviation from the normal evolutionary process

CALDER and PORRO (Johns Hopkins Hosp) report a typical case in a woman aged 34—evidently of the third group described above—which presented the picture of the Cushing pituitary syndrome (see Pituitary) The change had started four years earlier and showed coarseness of the skin, growth of hair on the face and body generally, great weakness, and instability of temperament Blood-pressure was high—190/130 The patient died Post-mortem examination showed adenoma of one adrenal and atrophy of the other The other endocrine organs appeared to be normal

HARE, ROSS, and CROOKE (London) also describe a case which was clinically indistinguishable from the syndrome attributed to basophilic adenoma of the pituitary A carcinoma of the adrenal cortex was removed at operation, but the patient died from shock Autopsy revealed a metastatic growth There was no sign of basophilic adenoma of the pituitary, but a slight hyaline change was observable in the basophilic cells of the anterior lobe

Another case, described by LESCHER and ROBB-SMITH, showed a similar syndrome A large adrenal tumour was removed at operation but the patient died soon afterwards The pituitary was normal It is shown that the adrenal syndrome is confined to women and tends to sex reversal, while the pituitary syndrome causes depression and inhibition Common to both are hypertension, disturbance of carbohydrate metabolism, and osteoporosis

The relation of overfunction of the adrenal cortex to hypertrichosis is discussed by NILES (New York) Excessive growth of hair is one of the symptoms in the syndrome just described as resulting from adrenal tumour, but Niles thinks that slight benign overfunction may produce hypertrichosis without the other and more serious symptoms developing He treated a number of such patients with irradiation of the adrenals, but the results were unsatisfactory. He is now investigating the subject further in order to see if any other gland is involved

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THE PITUITARY BODY.

THE name 'pituitary,' which means 'mucus secreting,' was given to this organ because it was originally regarded as responsible for the production of the nasal secretion Its other name, 'hypophysis cerebri,' means literally an outgrowth of the brain, which also is inaccurate This organ has been the subject of much research In 1894 Oliver and Schafer established its endocrine nature and demonstrated its action on the blood pressure Its relation to the genital organs was recognized by Frohlich in 1901, and in 1917 the pituitary body was shown to be essential to life Its therapeutic applications are matters of yesterday

The pituitary body is a small organ about the size of a pea, situated at the base of the skull in the sella turcica, and weighing about half a gramme It is attached to the floor of the third ventricle by *a short funnel shaped stalk, the infundibulum, this extends into* the posterior part forming the *pars nervosa*, which is covered with an epithelial layer called the *pars intermedia* In front of this is a vascular portion of a reddish colour, the *pars anterior* A portion of the gland extends along the stalk forming a sort of sheath this is the *pars tuberalis* In the middle of the pituitary body is a cleft —the *intraglandular cleft*—by which the organ may easily be divided into two parts The front portion consists of the pars anterior and is called the 'anterior lobe', the rear portion consists of the pars nervosa plus the pars intermedia, which together form the 'posterior lobe' The two lobes are distinct in function and

secretion; the posterior lobe contracts the uterus, raises the blood-pressure, and affects diuresis, while the anterior lobe promotes growth, secretes a sex hormone, and has other functions.

The relationship between the pituitary body and the other endocrine glands becomes more complicated as time goes on. Definite interaction has been demonstrated between it and the thyroid, the adrenals, the pancreas, and the sex glands. Indeed, so general is its influence that it has been called the 'master gland.' Most of its interglandular relations concern the anterior lobe and will be dealt with later.

Much of the recent work on the pituitary has been confined to either the posterior or the anterior lobe, and will therefore be dealt with later. One or two details concerning the pituitary as a whole may be mentioned before proceeding to deal with the lobes individually. JORES (Rostock, Germany) shows that in respect of hormone content the gland reacts to light and darkness. The hormones that influence the uterine contractions are considerably increased under the influence of darkness, and Jores thinks that this may explain the high incidence of births during the night. GIROUD, LEBLOND, and RATSIMAMANGA (Paris) have studied the ascorbic acid (vitamin C) content of the various parts of the gland and report that the greatest amount occurs in the pars intermedia; the anterior lobe has a fairly rich supply, but the posterior lobe contains comparatively little.

CORKILL (Melbourne) shows that the posterior lobe exercises an influence on carbohydrate metabolism while the anterior lobe bears a definite relation to fat metabolism. In these respects the gland appears to be linked with the pancreas on the one hand and with the adrenal cortex on the other. These points will be discussed more fully when dealing with the lobes separately.

Posterior Lobe.—The posterior lobe is the portion of the pituitary body about which our knowledge is more definite. The secretion of this lobe is known to possess certain definite properties: (1) It causes a rise in blood-pressure comparable to that produced by adrenaline, but more prolonged. (2) It excites contraction of certain involuntary muscles, notably those of the uterus and intestine. (3) It affects the secretion of the kidneys, on which it exerts a diuretic-antidiuretic effect. The exact physiological part played by the posterior lobe secretion is not fully understood, but it is believed that the pressor principle regulates the exchange of metabolites between the blood and the tissues, while the action on involuntary muscle may be directed on the uterus during parturition.

These properties of the posterior lobe determine the therapeutic employment of its extract. Its pressor properties have led to its use in combating shock; its action on plain muscle makes it useful as a stimulant of the uterus in labour or of the intestine in postoperative stasis; its diuretic-antidiuretic properties have found application in diabetes insipidus.

It is now known that the secretion of the posterior lobe contains two distinct principles—α-hypophamine or oxytocin, which acts on uterine muscle and has no pressor action, and β-hypophamine or vasopressin, which raises the blood-pressure but has no action on plain muscle Oxytocin is available commercially as *Pitocin*, vasopressin is marketed as *Pitressin* As a rule, for most purposes the extract of the entire lobe is used; it is only when one or other property is undesirable—as in cases of labour with high blood-pressure—that one of the special solutions is preferable

The only preparation of pituitary in the B P 1932 is *Extractum Pituitarii Liquidum*, or Pituitary (Posterior Lobe) Extract It is an aqueous extract and contains 10 units per millilitre The dose, by subcutaneous injection, is 2 to 5 units (0 2 to 0 5 ml) The U S P 1936 contains *Liquor Pituitarii Posterii*, or Solution of Posterior Pituitary, a very similar aqueous extract, the activity of which is based on a standard powdered pituitary The average dose is 15 minims or 1 c cm The dried gland also is official as *Pituitarium Posterium*, or Posterior Pituitary—no dose is given

The Pressor Principle—The pressor action of pituitary extract was first demonstrated by Oliver and Schafer forty-two years ago, and since then its use in combating shock and assisting low blood-pressure has been based on that knowledge, though its action appears to be too uncertain to justify its use in every case This uncertainty of action has led MELVILLE (McGill Univ, Montreal) to study the subject further, and he finds that the oxytocic hormone may inhibit or abolish the typical effects of the pressor constituent when both are present in the extract He concludes that under such conditions the action of the pressor hormone is to cause a fall of blood-pressure and to stimulate intestinal activity, while the oxytocic principle exerts a definite antagonistic influence in respect of these actions This, he thinks, may explain some of the conflicting reports on the clinical usefulness of these agents

A relationship with the thyroid appears to exist in connexion with the pressor principle GRUBER, MOON, and SUFRIN (Philadelphia) have shown that thyroid administration over long periods increases the sensitivity of the heart to the action of vasopressin STERN and GILLIGAN, however, find that the antidiuretic effect of the pressor principle is the same in patients with hypothyroidism as in subjects with normal thyroid function

The Oxytocic Principle—The oxytocic principle of the posterior pituitary probably acts physiologically in causing contraction of the uterus at parturition, and the extract is used therapeutically for that purpose During the early stages of pregnancy the uterus does not react to pituitary extract, probably because of the inhibiting effect of the luteal secretion Late in pregnancy, and particularly at parturition, the uterus reacts very strongly to this substance

Pituitary Extract in Labour—The general trend of opinion in regard to the use of pituitary extract in labour is that used judiciously

it is of distinct value, but that indiscriminate employment is fraught with danger. Too violent contractions may cause rupture of the uterus. Oversensitiveness to pituitary extract, though rare, is occasionally observed. SIMON and RYDER (Louisville) report five cases occurring in one hospital during two years, the symptoms being usually swelling of the face and hands with urticaria. Investigation showed that this was the result of specific sensitiveness, not to the pituitary hormone but to some other constituent of the extract.

The use of pituitary extract in labour may occasionally produce spasm of the cervix. According to COPELAND (Toronto), the timely injection of five minims of adrenaline solution will at once counter this should it occur.

The intravenous use of pituitary extract is advocated by BARON (Montreal), who has given it safely by this route in one-minim doses in a number of cases. The best results were obtained in patients in whom the membranes had ruptured, and in secondary inertia either before full dilatation or with full dilatation when the head was on the perineum. Good results have been obtained also in cases of post-partum haemorrhage and after caesarean section. The method has been unsuccessful in starting labour before term. WHITE and PRATT (Detroit) have studied the response of the uterus to intravenous pituitary extract during pregnancy and report that such injection carries no danger to the pregnancy or to the patient. The non-pregnant uterus shows no change in consistency, while the pregnant uterus shows a marked increase in consistency—a helpful aid though not a conclusive test for pregnancy.

The value of pituitary extract in post-partum haemorrhage is emphasized by RAWSON (Bradford). The extract should be injected into the fundus uteri, through the abdominal wall with a hypodermic needle, after the placenta has been expelled, provided the bladder is empty. To do this the uterus must be compressed bimanually, a fist being in the anterior fornix and the external hand behind the organ, pressing it forwards and upwards. Rawson reports a case in which this procedure caused immediate hardening without further relaxation, probably saving the patient's life.

Action on the Intestine.—RUNDLE (London) reports three cases of postoperative ileus in which pituitary extract given intravenously acted promptly in causing the bowels to move and averting a grave crisis. The dosage used was 0·5 to 1·0 c.cm. of pituitary (post. lobe) extract injected into the median antecubital vein very slowly—0·1 c.cm. every five seconds. In each case the result was dramatically sudden, free evacuation of flatus and faeces occurring almost before the injection was completed. In no case was a second injection necessary.

The action of pituitary extract on the intestine is utilized by VEIL (Jena) in the treatment of gall-stones. A subcutaneous injection of 10 Voegtlin units twice weekly, followed half an hour later by

a glass of aperient mineral water, caused his patient to pass fourteen stones in the course of three days

Diabetes Insipidus —It has been recognized for some time that the pituitary body is in some way associated with diabetes insipidus The nature of the relationship is uncertain, but it is known that therapeutic administration of posterior lobe extract has proved efficacious in many cases INGRAM and BARRIS (Chicago) have shown experimentally that faradic stimulation of the pituitary produces diuresis Subsequent examination of the pituitary in the experimental animals indicated that the point of application of the stimulus was on the superficial aspect of the anterior lobe close to the pars tuberalis

VEIL (Jena) remarks that in spite of the dramatic effect produced by administration of pituitary extract in some cases of diabetes insipidus, it has not been found possible to produce the disease artificially by experimental removal of the gland Among the aetiological factors of importance are fracture at the base of the skull, syphilitic meningitis or encephalitis and new growths of the pituitary growing up towards the base of the brain

HEALY (London) reports the case of a child aged 2½ years, where the cause was evidently tuberculosis of the pituitary Injections of pituitary extract controlled the polyuria and thirst, but the patient eventually died The cause of death was acute external hydrocephalus and acute tuberculous meningo-encephalitis—the terminal phenomena of a tuberculous infection of much longer duration The fact that diabetes insipidus appeared before other symptoms, and that pituitary disease had progressed to a greater extent than the tuberculous lesions elsewhere, suggests that the onset may correspond with the commencement of tuberculous infiltration of the pituitary

TURNER (Oklahoma) reports five cases of diabetes insipidus in which the comparative effects on the water balance of various pituitary preparations were studied Intermedin (the hormone of the pars intermedia) caused a reduction in diuresis and thirst in all cases The response was not so great as that obtained from equal doses of pituitary extract but it was free from pressor effects

A convenient method for administration of pituitary extract in diabetes insipidus is by application to the nasal mucosa Intranasal insufflation of ½ to 1 grain of powdered extract several times daily has been recommended, also use of the liquid extract diluted with normal saline as a nasal spray, or insertion in the nostrils of cotton pledgets soaked with 1 0 c cm of the extract

MAINZER (Vienna) describes seven cases treated by nasal insufflation Thirst disappeared in a few minutes, diminution of diuresis lasted from eight to ten hours and compensation was established on the second day In some cases treatment led to increased water tolerance, and smaller doses sufficed to control the symptoms SCHNEIDER (Berlin) also reports treatment by nasal insufflation The method, he finds, is inferior in efficacy to direct injection, but it is much more convenient to the patient

ALLEN and STOKES (Paterson, N.J.) report a case treated with the pituitary gonadotropic factor obtained from pregnancy urine and known as 'antuitrin-S' (*see* Anterior Lobe).' The patient was a boy, aged 11 years, who suffered from severe polyuria, polydipsia, and enuresis, and whose mental, physical, and sexual development was greatly retarded. Bilateral cryptorchism was present. He had been treated for two years with pituitary preparations without effect. In the hope that antuitrin-S might stimulate descent of the testes, a course of twenty-five injections of one c.cm. was given. About half-way through the course the symptoms of diabetes insipidus had disappeared and the testes were palpable. By the end of the course the changes in the boy were remarkable: his masculine characters had fully developed and the diabetes was completely cured (*see also page 198*).

Hormone of Pars Intermedia.—Reference was made last year (PRESCRIBER, 1935, May, 173) to the presence in the pars intermedia of a special hormone isolated by Zondek and Krohn, and called by them 'intermedin.' This hormone is distinct from vasopressin and oxytocin and its action differs entirely from that of either of these hormones. It has no influence on the basal metabolism, on the blood-pressure, or on the glycogen and fat contents of the liver, but it appears to reduce slightly the adrenaline content of the adrenals. It has some action on the water metabolism and has given striking results in a few cases of diabetes insipidus (see previous paragraphs), but its action in this respect is believed to be due to the presence of the posterior lobe principle. Intermedin has a specific action on the minnow (*Phoxinus laevis*), in which injection causes a characteristic red coloration at the point of attachment of the fins—an effect so specific as to serve as a means of standardization. Zondek claims to have isolated intermedin as a white powder with a dry weight of one microgram (0·000001 gm.) per phoxinus unit.

Gastrotoxic Factor.—In last year's review (PRESCRIBER, 1935, May, 174) reference was made to recent work by Dodds and associates showing the presence in the posterior lobe of a substance capable of inducing a severe lesion of the acid-bearing area of the stomach. This substance, the hydrochloride of which has been isolated as a water-soluble powder, acts in this way when injected subcutaneously; it is contained also in the B.P. extract of the posterior lobe, which has this effect when administered by mouth in large doses. The oxytocic principle alone does not have this effect, but the pressor factor has a definite action. The gastrotoxic factor is probably a distinct principle differing from the other hormones of the posterior lobe, but this is not yet definitely known.

More recent work by DODDS, HILLS, NOBLE, and WILLIAMS (London) shows that this may have a bearing on the causation of certain anaemias. Injection of pituitary extract causes a temporary inhibition of the acid secretion of the stomach which will not

respond to histamine for several hours After some days a severe anaemia develops, the blood count is greatly reduced and a reticulocytosis appears, indicating stimulation of the blood destroying system Further work is being done to investigate what appears to be a hormonal connexion between the posterior lobe of the pituitary, the stomach, and the blood picture

Confirmation of these findings comes from other sources LANGERON, PAGET, and DANES (France) find that subcutaneous *injection of pituitary (posterior lobe) extract has a temporary inhibiting action on the gastric response to histamine* Its effect on the acidity is marked but variable, and pituitary extract cannot be recommended as a remedy for hyperchlorhydria LUCCHESI and ZILIOLI (Parma) also observed that pituitary (posterior lobe) extract produced *acute lesions of the gastric mucosa* Prostration, loss of appetite and weight, and intestinal haemorrhage were noted, with necrotic haemorrhagic foci in the fundus of the stomach The blood showed an increase of chlorides and a diminution of red blood corpuscles

Carbohydrate Metabolism —That the posterior pituitary has an influence on carbohydrate metabolism is generally believed, but the exact nature of this influence is not understood The extract is known to be antagonistic to insulin and to relieve insulin hypoglycaemia CORKILL (Melbourne) states that he has found pituitary extract to be the best means of combating severe hypoglycaemia, one c cm subcutaneously showing its action in a few minutes It appears that the glucose-mobilizing effect is exerted on the liver-glycogen, but only in cases of emergency such as insulin hypoglycaemia Administered to a normal person it has no significant effect on the blood sugar

HILDEBRAND (Frankfort on-Main) claims to have found clinical evidence of hypopituitarism in disturbance of carbohydrate metabolism, and he concludes that in excessive glycogen storage the pituitary always plays an important part He suggests that the disordered carbohydrate metabolism of hypopituitarism may be associated with defective glycogenolysis

The antagonism between the pituitary and insulin suggests the *use of pituitary in the control of obesity* Insulin is known to effect an increase of weight in thin persons, and it has recently been shown by BLOTNER (Boston) that intranasal administration of pituitary extract causes a reduction of weight in obese persons Whether or not such treatment will be practicable remains to be seen

Anterior Lobe —Until about twelve years ago little was known of the function of the anterior lobe, and even now its exact relationship to the bodily functions is by no means clear The secretion of this lobe is known to be responsible for the promotion of growth, increased secretion before completion of growth producing gigantism, while if growth is completed before the oversecretion takes place the result is acromegaly Undersecretion results in dwarfism

A relationship has been demonstrated between the anterior lobe and the gonads. The anterior lobe secretes a hormone which stimulates the ovaries into activity, and another which is responsible for the development of corpora lutea. The relationship of the anterior pituitary to the sex glands is discussed in the section dealing with the Female Reproductive System.

Other interglandular relationships have been demonstrated; the anterior lobe appears to secrete adrenotropic, pancreatropic, thyrotropic, and lactogenic principles, all of which are in course of investigation. Some hold that these are not all separate hormones, and until more is known about them it is best to refer to them as principles or factors rather than as hormones.

LANGDON-BROWN (London) suggests that the anterior pituitary forms two basic secretions, one stimulating and the other inhibitory—a hormone and a chalone—the former being produced by the eosinophilic and the latter by the basophilic cells. These basic secretions are capable of chemical modification according to the needs of the body, and are then ready to stimulate or restrain the secretion of simpler hormones by the other endocrine glands, including the post-pituitary. It may be that the hormones circulate in an inactive form, becoming active, as Zondek suggests, only when they reach their destination. It is certain that their distinction is decided by some peculiar receptive capacity in the structure on which they act, but what determines that receptive capacity is not known.

The Growth Factor.—When the anterior lobe of the pituitary body is removed from growing animals, the most striking effect is complete cessation of growth, accompanied by a continuation of childish characters. This infantilism is seen in certain dwarfs, whose condition is the result of pituitary defect. In experimental animals the condition can be remedied by administration of anterior lobe extract. Collip has prepared a fraction of anterior lobe extract which appears to contain this factor without the others. This fraction, called 'Q-extract,' is said to be highly concentrated, maximal growth effects being obtained in test animals by daily administration of as little as one milligram of the dry substance.

SUSMAN (Manchester) maintains that the three types of cells in the anterior pituitary (see page 184) are phases of one type. An increased demand for the growth factor gives rise to an increase in the number of acidophilic cells, which represents an increase in the normal activity of the gland. There is also an emergency function which comes into play when the individual has been exposed to shock: then the number of chromophobe cells is increased. Thus the pituitary has a normal function in the control of cell growth and an emergency function best seen in connexion with shock.

The Adrenotropic Factor.—Another effect of removal of the anterior pituitary is atrophy of the adrenal cortex; the adrenal

medulla is not affected by such removal A fraction of anterior pituitary extract containing this adrenotropic principle and free from thyrotropic activity, has been prepared by Collip and co workers (Montreal) It is theoretically possible that some cases of Addison s disease may be due to pituitary failure, in which case the adrenotropic extract may be of service, indeed it is said to have effected improvement in reported cases

The Anterior Pituitary and the Pancreas—During the last few years much work has been done in establishing a relationship between the anterior pituitary and the pancreas, with results that promise to have an important bearing on diabetes That the anterior pituitary has some effect on the metabolism of carbohydrates and fats is evident A diabetogenic factor a ketogenic factor, and a pancreatropic factor have all been recognized, the diabetogenic factor is concerned with carbohydrate metabolism the ketogenic factor with fat metabolism and the pancreatropic with the secretion of insulin by the islets of Langerhans Whether or not these are separate principles is difficult to say In 1931 Houssay (Buenos Aires) showed that anterior pituitary contained a principle antagonistic to insulin In 1933 Barnes and Regan (Chicago) showed that in the absence of both pituitary and pancreas glycosuria did not occur until pituitary extract was injected Anselmino has shown further that extracts of anterior pituitary produce enlargement and increase in number of the islets of Langerhans this is probably a compensatory action aroused by the antagonism of the pituitary Animals from which the pituitary has been removed become very sensitive to the action of insulin and may even develop hypoglycaemia All this points very conclusively to a balance of action between the two glands any upset of this balance leading to hypo or hyperglycaemia according to the gland that happens to gain the ascendant

The presence of a ketogenic factor in the anterior pituitary has also been demonstrated In 1928 Burn and Ling (London) found that rats fed on a fat diet showed a greatly increased excretion of acetone bodies after administration of anterior pituitary extract This has since been confirmed in several quarters The name 'orophysin' has been suggested for this factor, but until more is known regarding it the simple term 'ketogenic factor' is preferable The principle is said to have been isolated, but this has not been confirmed The ketogenic factor is distinct from the thyrotropic principle Animals injected over long periods with ketogenic extracts have become resistant to its action and the serum of these resistant animals antagonizes the effect of ketogenic extracts in other animals The ketogenic factor increases the ketone bodies in the blood without influencing the liver glycogen, while the diabetogenic (carbohydrate metabolism) factor reduces the glycogen content of the liver without increasing the ketone bodies in the blood

The action of anterior pituitary extract on the blood sugar has been studied by VENKATACHALAM and RATNAGIRISWARAN (India)

Injection of an extract of the anterior lobe containing the growth promoting factor was found to increase the blood sugar to nearly twice its normal level Gonadal extracts reduce the blood sugar and counteract the rise due to anterior pituitary extract The vagal centre was made more sensitive to electrical stimulation by gonadal extract, whereas anterior pituitary extract had the opposite effect The hyperglycaemic effect of anterior pituitary extract is the result of its depressant action on the vagal centre, due possibly to stimulation of the thyroid

The Thyrotropic Factor—As already mentioned in the section dealing with the thyroid gland, a definite relationship seems to exist between this gland and the anterior pituitary It has been shown that removal of the pituitary produces subnormal thyroid function as evidenced by the very low basal metabolic rate In such cases injection of anterior pituitary extract quickly restores thyroid function This improvement does not last under continued injections of pituitary, in short a kind of immunity is produced On this principle an antithyrotropic serum has been produced which may prove useful in the treatment of hyperthyroidism This antithyrotropic substance has been shown to depress the metabolic rate, to antagonize the action of thyroxine, and to inhibit the action of the thyrotropic factor in normal and hypophysectomized rats It is believed that the thyrotropic principle found in anterior pituitary extracts is an entity having physiological properties distinct from those of the growth factor, the ketogenic principle, and the adrenotropic factor, and that it is not the same as the 'katechin' described by Blum and mentioned in the section dealing with The Thyroid Gland

Recent research by LOEB (St Louis) on the thyroid stimulating factor shows some very interesting results Injection of anterior pituitary in the guinea pig, he finds, causes changes in the thyroid gland with all the essential symptoms of Graves's disease Continued injection is followed by a return to the normal state The activity of the thyroid gland is associated with an increase of organic iodine in the blood Inorganic iodine ordinarily stimulates the thyroid, but if given with anterior pituitary extract the function of the thyroid is inhibited Iodine is known to inhibit the activity of the thyroid in Graves's disease A detailed account of the histological changes produced in the thyroid following injection of anterior pituitary extract is given by KIPPEN and LOEB These findings point to the significance of the anterior pituitary in the aetiology of Graves's disease, and if further developed might suggest a possible treatment for that condition

LEDERER (Louvain), as the result of work on the thyrotropic factor, concludes that underfunction of the thyroid and of the pituitary are usually associated, and that in such cases the signs of thyroid insufficiency frequently dominate the clinical picture, the symptoms being those of myxoedema One of the chief signs of

pituitary insufficiency is lowering of the B M R , a condition which may be relieved by injection of the pituitary thyrotropic factor

The condition of the pituitary in experimental cretinism has been studied by ZECKWER and associates (Philadelphia) Thyroidectomy in rats is followed by a stunting of body growth and the pituitary is increased in weight Its acidophilic cells are much reduced, the basophilic cells are increased, and a number of large cells containing hyaline substance appear The stunted growth is attributed to the loss of acidophilic cells from the pituitary

The Parathyroids—A certain relationship between the parathyroids and the anterior pituitary has been demonstrated by several workers Extracts of anterior pituitary have been found to cause a considerable rise in serum calcium The association of parathyroid adenomas with tumours of the pituitary has been observed Some workers claim to have isolated a parathyrotropic factor which causes proliferation of the parathyroid cells and hypertrophy of the glands A recent announcement is by HERTZ and ALBRIGHT (Boston), who say that the urine of patients with hyperplasia of the parathyroids contains a substance that produces a similar hyperplasia in normal rabbits MORLOG and MURPHY (Detroit) adduce evidence to show that in Paget's osteitis deformans the pituitary function is primary and that of the parathyroids only secondary

The Lactogenic Factor—Certain American workers claim to have isolated from the anterior pituitary a principle called by them 'prolactin,' which causes a secretion of milk in hypophysectomized and castrated animals This factor seems to be under control of the oestrogenic hormone during pregnancy, at parturition, with loss of the placenta, the level of oestrogenic substance drops sharply, permitting the release of the lactogenic factor of the pituitary The lactogenic factor has been tried clinically with reported success in women whose supply of milk had failed Trials in a number of castrated women with intact uteri are reported by WERNER (St Louis) In all cases the mammae became enlarged with signs of impending lactation, but none of the women lactated

Disorders of the Anterior Lobe—The anterior lobe contains three types of cells—acidophilic, basophilic, and neutrophilic or chromophobe—*each of which is capable, as in other glands, of* under- and over-function Dysfunction has been classified by CAMERON as follows —

Underfunction (1) Simmonds's disease, a general underfunction of the anterior lobe characterized by signs of premature senility (2) Pure anterior lobe deficiency (3) The Lorain-Levi, Fröhlich, and Laurence-Moon-Biedl syndromes, showing stunted growth and sex infantilism with obesity

Overfunction (1) Gigantism and (2) acromegaly, associated with tumours of the acidophilic (alpha) cells (3) Cushing's pituitary basophilism, associated with tumours of the basophilic (beta) cells (4) Amenorrhoea and disturbances of vision, associated with tumours of the chromophobe cells

To these must be added such disturbances as are brought about by departure from the normal balance of interactivity with other glands.

HAWKINSON (Brainerd, Minn.) reports a case of Simmonds's disease in a girl aged 17, who suffered from extreme cachexia. Injections of the anterior pituitary-like gonadotropic principle from pregnancy urine ('follutein') for four and a half months, with small doses of thyroid for a short time, effected wonderful improvement, to judge from the photographs accompanying the article. Hawkinson is of opinion that the entire anterior lobe is involved in Simmonds's disease, and that its hormone is stimulated by the gonadotropic substance. RAU (Berlin) reports a case of Simmonds's disease in a woman aged 56, who had completely lost her hair and showed other signs of pituitary cachexia. Treatment with dried anterior lobe (150 mouse units daily) caused the hair to grow again while the other symptoms improved. On stopping treatment, however, the symptoms returned. BERMAN (New York) reports treatment of twenty-four cases of this disease with anterior pituitary growth factor, with an average gain of 32 pounds and improvement in the general condition.

A case of the Lorain-Levi type of infantilism in a boy aged 16 is reported by DORFF (Brooklyn, N.Y.). The patient showed stunted growth, sexual infantilism, and delay in closure of certain epiphyses. Treatment with the growth factor ('antuitrin') resulted in a gain in height and weight, with full development of the sex characters, and the mental attitude was completely changed.

Pituitary Basophilism.—Cushing (Boston) has described a pluriglandular syndrome hitherto believed to be of cortico-adrenal origin, which was found to be associated with a pituitary adenoma composed of basophilic elements. Such cases exhibit characteristic features: (1) a peculiarly disposed adiposity; (2) a tendency to round shoulders, with lumbo-spinal pains; (3) a sexual dystrophy shown by early amenorrhoea in females and impotence in males; (4) a tendency to hairiness of the face and trunk in females and boys; (5) a dusky purplish appearance of the skin; (6) backaches, abdominal pains, etc. Most of these signs have hitherto been regarded as characteristic of disorders of the adrenals. The patients succumb to progressive enfeeblement associated in most cases with terminal infections. While such disorders may be associated with tumours of the adrenals, such a syndrome may occur in the absence of any alteration in the adrenal cortex, and this calls for examination of the pituitary in all cases. Several cases of adreno-cortical dysfunction, in which the symptoms resembled those of pituitary basophilism, are described in the section dealing with the adrenals. In these cases the symptoms suggested Cushing's pituitary syndrome, but the pituitary was found to be unaffected.

As the result of a study of the basophilic cells, BIGGART (Edinburgh) presents the following conclusions: The basophilic cell is a distinct morphological entity. Marked basophilic vacuolization

occurs in human castrates and in post climacteric glands, this appears to represent a functional and not a degenerative change The functional interpretation of anterior lobe basophilia appears at the moment impossible, but it seems probable that one of the functions of the basophil is the secretion of gonadotropic hormone

LANGDON-BROWN and SEWARD (London) describe a case of Cushing's syndrome presenting the three essential features—plethoric obesity, hirsuties, and amenorrhoea—in an unmarried woman aged 35 Other symptoms were raised blood pressure, albuminuria, lowered sugar tolerance, and kyphosis with bone pains Deep x ray therapy applied to the pituitary fossa caused headaches at first, but the condition improved later

Anterior Pituitary Therapy —The British Pharmaceutical Codex describes an extract of the entire lobe styled *Pituitary (Anterior Lobe) Extract*, and details its preparation and uses This preparation is available commercially as *Antuitrin* (Parke Davis), while a preparation of the sex-stimulating hormones is known as *Antuitrin S*, and one containing the growth factor is called *Antuitrin G* An extract of the anterior pituitary, standardized for gonadotropic and thyrotropic factors, is issued by Organon Laboratories under the name of *Ambinon* Extracts having gonadotropic effects are made from the urine of pregnancy, but these are believed not to be identical with extracts of the anterior pituitary and are therefore styled 'anterior-pituitary-like' preparations All these preparations are dealt with more fully in the section dealing with the Female Reproductive System Extracts containing the thyrotropic and adrenotropic factors, also the galactagogue principle (prolactin '), have been prepared by Allen & Hanburys, who offer these to research workers

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THE PANCREAS.

UNLIKE the glands already considered, the pancreas is not in itself an endocrine organ. It performs several functions, and the name 'ductless gland' is inapplicable. A certain portion of its tissue, however, is responsible for the elaboration of one of the most important hormones of the body—insulin.

Anatomy.—The pancreas is a racemose gland measuring from 12 to 15 cm. (4¾ to 6 inches) in length. The pancreatic duct, which conveys the digestive secretion, traverses the organ and is connected with the secreting alveoli by numerous ramifications. In the connective tissue between these alveoli are small groups of cells known as 'islets of Langerhans,' named after the German pathologist who first described them in 1869. These are minute endocrine glands, situated in, but apparently independent of, the pancreatic gland; they are scattered throughout the ordinary acinous cells of the pancreas, but are most numerous in the tail.

The pancreas thus produces both an external secretion—containing digestive enzymes—and an internal secretion or hormone. The relation of the pancreas to carbohydrate metabolism and to diabetes was studied as long ago as 1889, when von Mehring and Minkowsky discovered that its extirpation was followed by glycosuria and all the symptoms of diabetes mellitus. It was found later that ligation of the pancreatic duct caused atrophy of the acinous cells while the islets of Langerhans were not affected. Schafer, in 1913, was the first to suggest the presence of an internal secretion in the islets, and he named the hypothetical hormone 'insulin.'

FLORENTIN and PICARD (Nancy) have shown that the islets of Langerhans are very susceptible to other endocrine influence: at certain times the number of islets seems to increase temporarily. This is particularly noticeable during pregnancy, the gland reverting to its normal condition after delivery.

Insulin.—The assumption that diabetes was due to inadequate function of the pancreas led Zuelzer in 1908 to attempt treatment of diabetes by an extract of the pancreas. A certain amount of success attended his efforts, but it was soon found impossible to obtain an extract of pancreas free from digestive enzymes, which destroyed the hormone during extraction. In 1920 Banting ligated the pancreatic duct of dogs, and when the acinous cells were completely atrophied he extirpated the pancreas and extracted it with Ringer's solution. This extract gave immediately positive results by lowering the blood-sugar in depancreatized dogs. Further research permitted the production of insulin on a commercial scale, and in less than two years after its first isolation it was in use for treatment of diabetes the world over.

Insulin is now included in the British Pharmacopoeia. Two forms are official: solution and tablet form. The tablets are for

preparation of the solution and not for oral administration The official dose of insulin is from 5 to 100 units by subcutaneous injection The clinical use of insulin in the treatment of diabetes was fully reviewed in our issue of December last

A recent development in insulin therapy may be noted here During the past few years efforts have been made to retard the absorption of insulin in order to spread its action over a longer period An oily suspension has been suggested, also injection along with a vasoconstrictor substance (see PRESCRIBER, 1935, Dec , 373) Quite recently HAGEDORN and associates (Copenhagen) have succeeded in preparing a compound of insulin which is sparingly soluble in the tissue fluids This is protamine insulinate a combination of insulin with a protamine obtained from the sperm of a species of trout, *Salmo irideus* The *p*H of this compound approximates that of the plasma When injected considerable delay in absorption takes place, and the fall in blood sugar is much more gradual and persists for a longer time

Clinical trials of protamine insulinate in fifteen cases of diabetes are reported by ROOT and associates (Boston) The results generally confirm the findings of the Danish workers the lowering action on the blood sugar being more even and more prolonged than that following ordinary insulin Certain inconveniences in its use are noted ordinary insulin is best for morning use and the new compound for the evening Further, its use is contraindicated in coma, where rapid action is essential It must be remembered also that protamine insulinate is still in the experimental stage

LAWRENCE and ARCHER (London) confirm Root's results Protamine insulinate is much weaker in dealing with ingested carbohydrate, but its action on endogenous sugar is equal to that of insulin

LABBÉ (Paris) calls attention to the 'vegetable insulinoids'—substances of vegetable origin having the action of insulin One of these, the insulinoid of germinated barley (I G B), he has made the subject of careful study, and he reports that it has all the actions of insulin when administered by mouth or subcutaneously It lowers the blood sugar, diminishes acidosis, and improves the general condition The chemistry of this substance is rather obscure , it is not a guanidine derivative like synthalin, nor is it a vitamin

BABKIN (Montreal) asserts the existence of a close relationship between the blood sugar level and the external secretory processes of the pancreas Hyperglycaemia always increases the output of enzymes from the acinous cells and in certain cases increases the volume of the secretion Hypoglycaemia produced by the administration of insulin lowers the concentration of enzymes in the pancreatic juice After section of the vagus nerve this effect disappears

Hyperinsulinism.—Like other endocrine glands, the islets of Langerhans are subject to under- and over-functioning, leading to the conditions known as hypoinsulinism (or diabetes mellitus) and hyperinsulinism, its antithesis A condition called dysinsulinism, in which these two conditions alternate, has been known for some time As the islets of Langerhans control the blood sugar, hypoinsulinism (diabetes mellitus) is characterized by excess of blood-sugar necessitating treatment with insulin, while in hyperinsulinism the blood-sugar is below normal and constant ingestion of sugar is necessary to maintain its normal level Hyperinsulinism (or as some call it 'spontaneous hypoglycaemia') is analogous to hyperthyroidism; it was first recognized in 1927, and since then a number of cases have been reported

The symptoms vary with the degree of hypoglycaemia and are frequently mistaken for some other condition, indeed it was not until after the introduction of insulin that the condition became recognizable In addition to a reduction in the blood sugar, such signs as sweating, incoordination, and a sense of fear are the commonest features Convulsions and coma may occur in severe cases The causes are various hypoglycaemia may be due to excess of insulin, the result either of excessive administration or of tumours of the islets, or it may be the result of deficient opposing secretions, such as adrenaline Again, interference with the regulating centre has been suggested as a cause, as has also lack of glycogen Even in normal persons daily fluctuations of the blood sugar take place, and when these fluctuations increase beyond the normal safe curve it is possible that the pancreas is temporarily overworking

Recent reports show that an attempt is being made to classify the cases of hyperinsulinism according to the apparent cause and to institute treatment accordingly RABINOWITCH and FOWLER (Montreal) studied the blood-sugar and respiratory curves in five cases The respiratory metabolism following injection of glucose showed either oxidation or storage when the glycogen was low the tendency was towards storage, when the diet was liberal the tendency was towards oxidation The condition, they think, resembles insulin shock SCHUR and TAUBENHAUS (Vienna) point out that administration of sugar is merely symptomatic treatment and does not get at the cause When this is a tumour of the pancreas, surgical intervention is called for, but in many cases the cause is obscure GOLDZIEHER (New York) reports 112 cases, of which 88 showed signs of hypopituitarism and 20 were hypothyroid These were treated with appropriate glandular therapy and dietetic measures JOHN (Cleveland), whose previous report was recorded two years ago (PRESCRIBER, 1934, May, 190), again refers to treatment with insulin It is only the functional type, that is, a deranged mechanism of insulin production, that responds to this treatment it is useless in cases of pancreatic tumour John reports three cases so treated with success, the dose being 20 units half an hour after

meals, with a high fat diet. Insulin may be used to diagnose between the functional and the surgical types.

Other Pancreatic Hormones.—In the opinion of some the pancreas has other functions besides the supply of digestive enzymes and the secretion of insulin. In 1928 Frey and Kraut, German workers, described a 'circulatory hormone' which they had extracted from the pancreas; this is now obtainable commercially under the name of *Padutin* (Bayer). In 1929 Gley and Kisthinios, of Paris, prepared an insulin-free extract of the pancreas also capable of reducing blood-pressure and having a favourable influence in cases of angina pectoris. This they called *Angioxyl*. These substances both have the property of reducing blood-pressure when given intravenously, and their action is sufficient to inhibit the pressor action of adrenaline.

THEISEN (Cologne) reports treatment of seven cases with padutin, the cases including Raynaud's gangrene, trophoneurotic disturbances, acroparaesthesia, and gangrene of the extremities. All were greatly improved.

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THE FEMALE REPRODUCTIVE SYSTEM.

NO department of endocrinology has received so much attention during recent years as that concerning the reproductive organs. The intimate relationship between the sex organs and the anterior pituitary has given the subject an added interest and has clarified much that has hitherto been obscure.

The Ovary.—The ovary consists of a stroma or framework, in the meshes of which are embedded a number of vesicular (graafian) follicles. After puberty these follicles increase in size and a cavity is formed filled with liquor folliculi. The mature follicle ultimately

bursts and the escaping ovum is conveyed by way of the uterine (fallopian) tube to the uterus—a process which proceeds without interruption from puberty to the menopause After discharge of the ovum, a series of changes occurs within the follicle, resulting in the formation of the corpus luteum If the discharged ovum is fertilized, the corpus luteum increases in size during pregnancy, after which it becomes again reduced, if the ovum is not fertilized it dies, the corpus luteum degenerates, and the menstrual flow begins

The endocrine process involved is as follows At the end of each menstrual period the immature follicle is acted upon by one of the gonadotropic hormones of the anterior pituitary (prolan A or rho I) which causes it to ripen At the same time the ovary secretes a hormone (oestrin) which stimulates the uterine musculature until about the fourteenth day, when the follicle ruptures, releasing the ovum Then another gonadotropic hormone from the anterior pituitary (prolan B or rho II) effects luteinization of the ruptured follicle forming the corpus luteum The corpus luteum itself secretes a hormone (progesterone), which collaborates with oestrin and prepares the mucous membrane for the nidation of the ovum During pregnancy large quantities of the anterior pituitary hormones appear in the urine

Thus it will be seen that at least four hormones are concerned in the reproductive cycle The placenta also probably secretes a hormone The exact nature of these hormones will be discussed later

Among the more recent developments may be mentioned the close kinship that has been established between the hormones of the male and female gonads also a chemical relationship that has been demonstrated between these hormones and certain sterols, certain vitamins, and certain carcinogenic substances This last promises a new conception of the origin of cancer

The cause of menstrual bleeding has hitherto been believed to be due to withdrawal of oestrin Engle, Smith, and Shelesnyak (New York) have found, however, that the cause is probably the withdrawal of progesterone of the corpus luteum Experimental menstruation in animals can be prevented by administration of this hormone, the flow returning on withdrawal of progesterone Observations on human beings show that the menstrual flow occurs in the presence of a high oestrin content of the blood Allen and Reynolds (New York) show that progesterone has dual properties—endometrial proliferation and inhibition of uterine motility

Reynolds (New York) holds that oestrin is essential to the act of parturition He adduces as evidence the specific motility inducing property of oestrin on the uterus of animals and of human beings and its presence in increasing amounts during gestation, its highest level being reached at the onset of labour The action of oestrin is held in abeyance by the antagonistic action of progesterone and probably also by the gonadotropic hormones of the pituitary, but at the time of labour the oestrin is sufficient to overcome the inhibiting force These views have been confirmed experimentally

Carcinogenesis.—The possible relationship between the oestrogenic hormones and cancer has already been mentioned. The chemical nature of these hormones is now well understood, their relationship to ergosterol and to vitamin D has been fully worked out, and a similarity in molecular structure to certain cancer-producing hydrocarbons has been demonstrated. CRAMER and HORNING (London) have produced experimental pituitary tumours and mammary cancer in mice by the administration of oestrin, though only after very prolonged application corresponding in man to a period of nearly ten years. MCEUEN, SELYE, and COLLIP (Montreal) report a very similar experience, and ZONDEK reports that a large pituitary tumour was formed in a female rat by the same process. These pronouncements have led to a fear that oestrin, especially if administered in large doses, might be capable of inducing malignant changes. Such fear appears to be groundless. The subject has been ably reviewed by DODDS (London) and by LOEB (St Louis). Dodds shows that the similarity in chemical structure between the carcinogenic hydrocarbons and oestrin is not so close as it is between the male and female sex hormones (the difference in the latter case is only one hydrogenated carbon ring), yet no one would ever suggest that injection of oestrin might induce male changes in women. Loeb shows that the oestrogenic hormones are limited in their action to the tissues in which they induce growth processes during the normal sexual cycle. The mechanism by which the hormones produce proliferative processes in the sex organs differs from that underlying cancerous transformation. The real importance of this discovery lies in its presentation of a new outlook in regard to the aetiology of cancer and a new direction for cancer research.

Pituitary-Ovarian Relationship.—As already shown, the anterior pituitary secretes two hormones necessary for stimulation of the ovaries into activity and for the development of the corpus luteum. The excretion of these hormones in the urine during pregnancy is the basis of the well-known pregnancy tests, which will be dealt with later. An enormous amount of work has been done in establishing the pituitary-gonad relationship, the main points of which were briefly explained in the opening paragraphs of this section.

More recently a definite relationship between the ovarian follicular and the *posterior* pituitary hormones has been established. ROBSON (Edinburgh) has shown that the ovarian hormone sensitizes the uterine muscle to the oxytocic action of the posterior pituitary, while a certain synergism between oxytocin and oestrin has been demonstrated by MARRIAN and NEWTON (Toronto). Although information is as yet incomplete, it may be said that oestrin definitely acts on the non-pregnant and pregnant uterus, causing hypertrophic growth of the endometrium and growth and development of the uterine muscle. It increases the reactivity to oxytocin of both types of muscle as well as the spontaneous rhythmic contractions. The sequence of events gives at least presumptive evidence of a function in the normal termination of pregnancy.

That the balance between the anterior pituitary and the gonads is not all on one side is shown by ZONDEK (Univ of Jerusalem) who presents evidence of an inhibiting effect of oestrin on the pituitary hormones Experiments on rats prove that administration of oestrin in large doses over long periods inhibits the gonadotropic hormones of the pituitary by preventing the formation of corpora lutea, and destroys the effect of the growth hormone, producing dwarf animals His work is only preliminary and Zondek promises to report further on the significance of these findings Experiments by FLUHMANN (San Francisco) point to a somewhat similar inhibiting effect, attributed by him to the formation of 'antihormones'

The close functional relationship between the pituitary and the gonads is well brought out in two clinical reports from America MAZER and SPITZ (Philadelphia) record successful results from irradiation of the pituitary in a number of cases of amenorrhoea and other functional menstrual disorders The procedure appears to be harmless COLLINS, THOMAS, and MENVILLE (New Orleans) report that irradiation of the pituitary affords lasting relief from menopausal symptoms Their experience points to an increased secretion of the gonadotropic hormone at that time, the result of ovarian atrophy and consequent decrease of oestrin

Therapeutic Applications—During the past year a conference was held in London under the auspices of the League of Nations to consider the question of standardization of the sex hormones At that meeting a uniform scientific nomenclature and standard units were adopted for three important products—the oestrogenic hormone, the hormone of the corpus luteum and the male sex hormone Referring to this matter the Annual Report of the Medical Research Council contains the following remarks 'No conference was more needed The market is flooded with different preparations of the various sex hormones, and each manufacturing firm has given a proprietary name to its own particular product While some of these preparations are good, others are of a semi-bogus nature The situation lent itself to quackery and to ignorant treatment of disease, a condition of affairs unfortunate alike to manufacturing firms of high repute and to the general public'

The preparations in general use therapeutically are the oestrogenic hormone, the corpus luteum hormone, the pituitary gonadotropic hormones, and the placental hormone The male sex hormone will be considered in another section

Oestrogenic Hormone—Oestrin is the generic name applied to the oestrus producing hormone of the ovaries it comprises more than one substance The parent substance is the saturated hydrocarbon oestrane, of which three derivatives are known The names adopted for these by the conference already referred to are *Oestrone*, a ketohydroxy derivative, *Oestradiol*, a dihydroxy derivative, *Oestriol*, a trihydroxy derivative The international standard is crystalline oestrone The principal commercial products representing these compounds are the following —

Oestrone: Menformon (Organon Labs.); Oestroform (British Drug Houses); Progynon (Schering); Theelin (Parke Davis); Unden (Bayer).

Oestrone Benzoate: Dimenformon (Organon Labs.); Oestroform-B (B D.H.); Progynon-B (Schering).

Oestriol: Theelol (Parke Davis).

These products occur in crystalline form and are usually obtained by extraction from pregnancy urine; more recently from the ovary itself. They differ but slightly in their individual action, and so far their use is to some extent empirical. The unit of activity is the specific oestrogenic activity possessed by 0·1 γ (0·0001 mg.) of standard oestrone: one milligram ($\frac{1}{64}$ grain) thus represents 10,000 units. Oestrone and oestrone benzoate are used for similar purposes: the benzoate is soluble in oil and is capable of being given in larger doses; it is slowly hydrolysed in the body and its action is spread over a longer period. Both are usually supplied in solution for intramuscular injection; oestrone also in tablets for oral administration. *The dosage ranges from 500 to 50,000 units or more.*

Several other reliable ovarian products are available. Among these may be mentioned *Agomensin* (Ciba), the hydrosoluble ovarian substance, and *Sistomensin* (Ciba) the liposoluble ovarian hormones. Both are prepared from whole ovaries including corpora lutea.

The action of oestrone when injected into a female animal is to produce those changes which facilitate the fertilization of the ovum. Oestriol has a similar effect but less intense. The employment of these products in therapeutics is restricted mainly to female complaints, especially disorders of menstruation and of the menopause, but they have given good results in certain other conditions, such as gonococcal vaginitis in children. They have been tried in haemophilia on the ground that women never suffer from this complaint; reports are conflicting and their value in this condition is at best doubtful. The following are some of the more recently recorded clinical reports.

MAZER, MERANZE, and ISRAEL (Philadelphia) find that injections of from 100,000 to 200,000 units, given in divided doses over several months, have no appreciable effect on body-weight, B.M.R., blood-pressure, etc., but in six cases a delay of from one to three weeks was observed in the menstrual flow, with establishment of a new date of onset. This they attribute to a temporary inhibition of the anterior pituitary, which normally controls the menstrual function.

WILLIAMS (London) speaks well of the value of oestrone in the menopause. Many cases improve considerably on doses of 10,000 units weekly. Itching is relieved, flushes disappear, and mental depression is overcome.

WATSON (Toronto) mentions its value in atrophic conditions of the reproductive tract. Sex hormone therapy is contraindicated in such conditions as malnutrition and anaemia: the patient must be well nourished and in good health or the treatment will have no effect.

KURZROK, WILSON, and CASSIDY (New York) report good results

in the treatment of amenorrhoea Dosages of 100 000 units or more are necessary in cases of primary amenorrhoea, and about 50,000 units in secondary amenorrhoea

MONCRIEFF (London) tried the effect of oestrone and of oestriol in stimulating the metabolism and increasing the weight of prematurely born infants A certain amount of improvement was observed in some cases, but the results were not definite enough to warrant its use as a routine method

ROBINSON, DATNOW, and JEFFCOATE (Liverpool) tried the effect of oestrone in producing abortion in a number of cases in which therapeutic abortion was indicated In early pregnancy it had no effect whatever, and later its action was very unreliable It is, however, the best method of evacuating the uterus in cases of missed abortion or intrauterine death of the foetus and it may prove of value in dealing with primary uterine inertia

The effect of oestrone on the human vaginal mucosa has been studied by LEWIS (New Haven Conn) who finds that it produces vacuolization and multiplication of certain layers of cells This is particularly evident in the newborn and in children In this connexion MILLER (Hartford, Conn) reports two years' experience of its use in treating gonococcal vaginitis in children and finds that the condition is cleared up more or less promptly Relapses may occur, but these are frequently due to reinfection from the urethra TE LINDE and BRAWNER (Johns Hopkins Univ) state that in their experience the oestrogenic hormone given orally or hypodermically is of no value in gonococcal vaginitis Solution in oil proved effective in about 70 per cent of cases and administered in the form of a pessary it was effective in all cases The preparation used was amniotin (Squibb) A note of warning is sounded by WITHERSPOON (Tulane Univ , New Orleans) who deprecates the administration of sex hormones to young girls It may affect their future development , it does not reach the cervix which may still retain the infection , further the hypodermic method is inadvisable for young children The potential dangers of the method must not be overlooked

A case of pre adolescent eunochoidism is reported by LISSER (San Francisco) The patient was a girl aged 17 whose secondary sex characters were entirely absent Ovarian therapy (agomensin, progynon, and theelin) caused the secondary sex characters to appear, and after three years' treatment the patient was entirely normal

COLLENS and associates (Brooklyn) have tried oestrone in diabetes The anterior pituitary antagonizes insulin and oestrin antagonizes the anterior pituitary They find that administration of oestrone partially prevents the development of diabetes following pancreatectomy, but it has no effect on the tolerance of the diabetic patient

The Corpus Luteum —The hormone of the corpus luteum is now known as *Progesterone* The crystalline hormone has been

isolated in pure form; it is a diketone and exists in two forms—α-progesterone and β-progesterone, both having the same formula, $C_{21}H_{30}O_2$, but differing in their melting points. The commercial product is standardized according to its activity in causing proliferation in immature rabbits previously treated with oestrin. The leading commercial preparations are:—

Progestin (B.D.H.): ampoules, 2 rabbit units per c.cm.

Progestin (Organon): ampoules, 1 rabbit unit per c.cm.

Proluton (Schering): ampoules containing ½ to 5 international units (an international unit=1⅔ rabbit units).

Lutren (Bayer): ampoules containing 2 rabbit units.

Progesterone preparations are administered by intramuscular injection: orally they are without effect. The usual dose is 1 to 2 rabbit units. Its principal application is in habitual or threatened abortion; it is also of value in menstrual disorders. In some cases it is advisable to combine the treatment with oestrone.

A suggestion has recently been made to use the corpora lutea of whales for the production of progesterone. The glands in the whale are very large, and if used would help to reduce the present high cost of this product.

FALLS, LACKNER, and KROHN (Univ. of Illinois) report on the value of progesterone in habitual and threatened abortion. They treated with success 34 out of 41 such cases with the hormone. One rabbit unit completely inhibits human uterine contractions in a seventh-day parturient patient, and nullifies the effect of one c.cm. of pituitary (post. lobe) extract.

CAMPBELL and HISAW (Univ. of Wisconsin) found that progesterone gave temporary relief in a small series of cases of dysmenorrhoea. Their results were not sufficiently conclusive to warrant a general statement, but they recommend its use in selected cases.

Pituitary Gonadotropic Hormones.—As already mentioned, the anterior pituitary secretes two hormones having an influence on the ovary—prolan A or rho I, the follicle-stimulating factor, and prolan B or rho II, the luteinizing hormone. These hormones are present in large quantities in the urine of pregnancy, which is their usual commercial source. As they are not obtained direct from the pituitary they are styled 'anterior pituitary-like' preparations. They are standardized in rat units, according to their power to cause the formation of corpora lutea in immature rats. The following are the principal products on the market:—

Antuitrin-S (Parke Davis): 100 rat units per c.cm.

Ambinon (Organon): an extract of anterior pituitary containing gonadotropic with a variable amount of thyrotropic hormone. Ampoules, 50 'synergic units' per c.cm.

Pregnyl (Organon): dry powder prepared from pregnancy urine. Ampoules: 30, 100, and 500 rat units.

(In practice 1 c cm of ambinon is usually given with 100 rat units of pregnyl from a twin ampoule for gonad stimulation Where a non gonadotropic effect is primarily required ambinon can be used alone)

Gonan (B D H) dry powder prepared from pregnancy urine 100 rat units per ampoule, with an ampoule of d stilled water for preparing a fresh solution

Prolan (Bayer) pellets 150 rat units ampoules 100 and 500 rat units

The chief therapeutic indications of the anterior pituitary like preparations are sexual underdevelopment as delayed puberty, infantilism undescended testes insufficient follicle stimulation as in functional amenorrhoea and oligomenorrhoea insufficient corpus luteum stimulation as in menorrhagia and metrorrhag a They are given by intramuscular injection

HENDERSON (Toronto) reports treatment of 39 cases of menor rhagia and metrorrhagia by means of anterior pituitary like hormone 31 were relieved of menorrhagia and 25 had complete return to normal In those unaffected the condition was not due to endocrine dysfunction This preparation is of distinct value in cases due to endocrine imbalance and when there are no pathological lesions in the genital tract

HICKS and HONE (Adelaide) describe a case of extreme wasting associated with amenorrhoea Anterior pituitary dysfunction was diagnosed and 100 units of prolan (Bayer) given intramuscularly The circulatory response was evident in twenty four hours

STARR and PATTON found that antuitrin S (one c cm daily or thrice weekly) caused remissions in hyperthyroidism in young women In older women or in cases where the ovarian function had been interfered with by disease or by operation the results were unsatisfactory

Acne —There being evidence that acne vulgaris in the adolescent is due to endocrine imbalance LAWRENCE and FEIGENBAUM (Boston) treated fifteen patients with antuitrin S with good results In a later paper, LAWRENCE describes a further series of cases in which the response was very satisfactory the acne cleared up and where genital hypoplasia existed this became normal at the same time Lawrence concludes that it is highly probable that the imbalance involves the anterior pituitary gonadal mechanism

Undescended Testes —A number of reports refer to the treatment of undescended testes anterior pituitary like hormone being evidently as effective in the male as in the female The reports include a certain number of failures and it is noted that unless the condition is due to underfunction of the pituitary the treatment will be un availing and surgical intervention will probably be necessary This point is emphasized by SEXTON (St Louis) who treated thirteen boys with genital underdevelopment of varying degrees cryptorchism being present in four The majority were benefited FETTER

used prolan in five cases of cryptorchism, with good results in three. SPENCE and SCOWEN (London) used pregnyl in thirty-three cases (ages 4 to 26 years) in doses of 500 rat units twice weekly. Again the majority showed good results. WEBSTER (New York) reports eleven cases with complete descent in ten. SIPPE (Brisbane) reports a case in which antuitrin-S effected descent in a boy aged 10 years. GOLDMAN, STERN, and LAPIN (New York) treated eleven boys with only one failure. KOPLIN (Los Angeles) reports a case in which treatment had to be stopped on account of glycosuria which supervened. (See also page 179.)

Pregnancy Tests.—As already stated, the anterior pituitary secretes gonadotropic hormones which are found in abundance in the urine during pregnancy. This excretion begins at a very early stage of gestation, and the presence of the hormone in the urine is diagnostic of pregnancy. Inoculation of immature mice with the urine of a pregnant woman causes signs of maturity to develop rapidly: the ovaries of the animals are covered with red spots—corpora haemorrhagica or *blut punkte*. This test is known as the Aschheim-Zondek test and has proved very reliable. In addition, other tests have been devised on somewhat similar principles, and some of these are promising.

CREW (Edinburgh) finds that the A.-Z. test invariably gives a definite and presumably permanent negative result ninety-six hours after normal and complete parturition, and he suggests its routine use on the fifth day of the puerperium for the diagnosis of retained living products of conception.

SMITH (Glasgow) shows that the A.-Z. test is of value in conditions other than pregnancy. He reports two cases of chorion-epithelioma which were diagnosed by this test, unfortunately too late to save the lives of the patients.

SCHMULOVITZ and WYLIE (Baltimore) describe a chemical test by which the presence of oestrone may be detected in the urine. They think that the test may be of service also in the diagnosis of impending eclampsia, as the excretion of oestrone is much diminished in the toxaemias.

Last year (PRESCRIBER, 1935, May, 189) reference was made to a test devised by Kanter and co-workers, of Chicago. A fish, the Japanese bitterling (*Acherlognathus intermedium*), is the test object, and when 4 c.cm. of the pregnancy urine is placed in the tank the ovipositor shows marked growth in 24-72 hours. KLEINER, WEISMAN, and BAROWSKY (New York) have subjected this test to exhaustive trials and report that it is not specific. Only nine out of twenty-one pregnant urines gave definitely positive reactions.

Friedman's modification of the A.-Z. test has been tried by LEWIN (Johannesburg), who reports that it is not reliable.

RENTON (Durban) describes a new test based on the presence of histidine in the urine. He tried it in 100 cases and claims to have obtained positive results in all, including early cases.

The Placenta.—During recent years much work has been done by Collip and associates (Montreal), and it is now known that the placenta stores or elaborates three different principles—oestrone (ether-soluble), emmenin (alcohol-soluble), and an anterior pituitary-like principle, 'A-P-L' (alcohol-insoluble), resembling prolan A. Emmenin and A-P-L both promote oestrus in immature female rats, but while emmenin has no effect on males, A-P-L promotes the growth of accessory sex glands. All three are excreted in the urine during pregnancy. Emmenin is an ester of oestriol, the trihydroxy derivative referred to in a previous paragraph, and has oestrogenic properties. It has not been isolated in pure form like oestrone, but an active extract containing emmenin has been prepared which is effective, when given orally, in dysmenorrhoea, amenorrhoea, and post-menopausal symptoms.

Recent experiments by SELYE, COLLIP, and THOMSON (Montreal) show that ovariectomy during gestation does not interfere with the life of the placenta: it terminates pregnancy only because it causes the death of the foetus. The placenta is independent of the ovarian hormones, and it appears that the length of the gestation period is determined by factors inherent in the placenta.

According to BOYD (Kingston, Ontario) the placenta plays a part in the fat metabolism of the foetus It appears that the actual tissue substance of the placenta is actively engaged in transferring at least a part of the lipoids from the mother to the embryo in the latter part of gestation.

Therapeutic Applications.—Under the name of *Emmenin* a placental extract is issued by an American firm. A British preparation, *Emmenoplex* (Glaxo Labs), is a standardized preparation of emmenin prepared according to Collip's method; it is given orally in doses of 60 to 240 minims daily to supplement the oestrogenic activity of the underfunctioning ovary in cases of menopausal disturbance, dysmenorrhoea, menstrual headache, and oligomenorrhoea. An extract of human placentas, known as 'immune globulin' or 'placimmunin,' has been used in America as a prophylactic against measles, apparently with some success.

The clinical use of emmenin (Collip) is recorded by GOLDBERG and LISSER (San Francisco), who have tried its effect on 66 patients. It has proved helpful in restoring menstruation if periods have been absent for less than a year, but is probably useless after a longer period. In oligomenorrhoea the menstrual interval was more nearly regularized. Polymenorrhoea was unaffected. Hypomenorrhoea was improved in nine out of twelve cases. Menopausal symptoms were relieved in a fair majority of cases. In two out of four cases of sterility pregnancy occurred under emmenin treatment. Severe dysmenorrhoea was remarkably relieved in thirty out of forty cases: this appears to be its most significant clinical usefulness. The only drawback to its use at present is its cost.

WATSON (Toronto) reports the use of emmenin in dysmenorrhoea,

over 150 patients coming under his observation Emmenin, he finds, is a valuable form of supplementary hormone therapy when the pains are due to forcible uterine contractions Other treatment is necessary according to the patient's condition, such as iron, diet, and rest. Complete relief was obtained in forty-nine cases, of which twenty-one have shown no return of symptoms In addition many patients experienced very gratifying partial relief

The use of placental extract for the prophylaxis and treatment of measles was first reported by McKhann and Chu in 1933, and has recently been the subject of further reports The extract is made from human placenta and is adjusted for protein-nitrogen strength It is known as 'immune globulin (human)' or 'placimmunin' McKHANN, GREEN, and COADY (Boston) report that intramuscular injection either prevents the disease or causes it to appear in a modified form This is confirmed by LEVITAS (Westwood, N J), who finds that it is of definite value also in treatment (*see* PRESCRIBER, 1936, Jan , 18)

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THE MALE GONAD.

THAT the testis has a function beyond that of production of spermatic fluid has long been recognized: the effects of castration on the entire organism are too well known to require enlargement. Recent work has demonstrated that the testis secretes at least one hormone, which has been sufficiently purified to yield crystals of high potency. Secretion of this hormone appears to be controlled to a great extent by the pituitary. The hormone, which is excreted in the urine, is called *Androsterone*. It is obtainable from human urine or from the testes of mammals.

Synthetic androsterone has been prepared from cholesterol: this is chemically identical with the hormone obtained from urine—$C_{19}H_{30}O_2$. It has the property of stimulating comb growth in capons, and this property is used as a basis of standardization. It also causes growth of the accessory reproductive glands of mammals.

KORENCHEVSKY and DENNISON (Lister Inst., London) have studied the effect of injections of testis hormone, both that extracted from human urine and synthetic androsterone, and of oestrone on normal and castrated rats. Their results show that these substances are not merely sex hormones but have manifold effects influencing other important functions and organs. Further work by KORENCHEVSKY, DENNISON, and SIMPSON on androsterone and its derivatives has a more or less technical significance and need not be abstracted (*see* References).

The biological effect of androsterone has been studied by several workers. GREENWOOD, BLYTH, and CALLOW (London) report on several technical points connected with the quantitative response and the effect of variables. CALLOW and PARKES (London) find that rapid growth of the comb follows injection of 2·5 to 5 mg. daily, and that the comb can be maintained at normal level by daily doses of 1 mg. CALLOW and DEANESLY studied the effect of androsterone on castrated animals and conclude that certain urine concentrates may contain a male hormone other than androsterone and having a much greater activity per capon unit on the accessory

glands of mammals. In a further communication the same workers report trials with dihydro-androsterone (andradiol) and androsterone benzoate. Andradiol is about three times as active on the capon comb as androsterone, but its activity on the accessory glands is low compared with that of urine concentrate. Androsterone benzoate appears to be inactive, unlike the corresponding benzoate of oestrone.

This work has led to the announcement—made quite recently—that the testis contains another and much more active hormone. A crystalline steroid, called *testosterone*, has been isolated from testis extracts and has since been prepared artificially from cholesterol by several workers independently. DEANESLY and PARKES (Nat. Inst. Med. Research) report on testosterone. They say it is seven times more active on capons than androsterone; it is more than twice as active on the prostate, and ten times as active on the seminal vesicles. Its derivatives, methyl-testosterone and testosterone benzoate, have also been studied. The methyl derivative is less active on capons but more active on rats than testosterone; the benzoate is comparatively inactive. Laqueur and others have shown that testosterone is activated by an *x*-substance, probably a fatty acid, obtainable from testis tissue. This has been confirmed by DEANESLY and PARKES, who show that the activity of androsterone can be greatly increased by administration with an increased amount of oil or with added palmitic acid. Artificial androsterone and artificial testosterone, supplied by Ciba Ltd, were used in these investigations. These products are not yet on the market, but it is expected that testosterone will be before long.

Clinical Applications.—The real function of the testis hormone (or hormones) is to control the accessory reproductive organs: it is not a stimulant of the male sexual function. Consequently androsterone has not yet found any very definite clinical applications. Its use in the treatment of enlarged prostate has been suggested by LOWER (Cleveland), while DIETEL (Erlangen) claims to have successfully treated a number of cases of enuresis with testicular extract. Beyond these and a few tentative suggestions, little has as yet been heard of androsterone as a therapeutic agent.

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OTHER ENDOCRINE ORGANS.

A FEW minor glands and organs remain to be considered In most cases the endocrine nature of these is doubtful, but as all have at some time or other been mentioned in this connexion they may be passed briefly in review

The Heart and Circulation.—The idea that the heart-beat is controlled by some principle—probably a hormone—has been gaining ground during the last ten years In 1924 Haberlandt, of Innsbruck, first demonstrated the presence in heart-muscle of a stimulating substance, which he called ' heart hormone ' (*Herzhormon*) Following closely on Haberlandt's work is that of Schwartzman, who showed that extracts of ordinary muscle are capable of similar action on the heart-beat and circulation Further, Zuelzer has shown that the liver contains a principle useful in anginoid conditions, and the same property has been attributed to certain preparations of the pancreas Cannon also has described a new hormone, similar to adrenaline, obtainable from certain muscles The result is quite a confusing series of ' circulatory hormones,' which include Haberlandt's preparation *Lacarnol*, Schwartzman's *Myoston* or *Myol*, Cannon's new hormone *Sympathin*, Zuelzer's liver principle *Eutonon*, and the pancreatic principles *Padutin* and *Angioxyl* already described

Recent work on these products, while in many respects confirming the claims made for them, shows a tendency to discount their endocrine nature BARKER, BROWN, and ROTH (Rochester, Minn), in a study of the effect of tissue extracts in intermittent claudication, express the opinion that their effect is not due to vasodilatation but to some agent producing muscle contraction HEINSEN (Wurzburg) says that the liver preparation ' eutonon ' owes its action to tyramine and choline

The Liver.—Though the action of liver diet and liver extracts in pernicious anaemia and in some other conditions suggests the

presence of a hormone, the liver has not been classed as an endocrine organ In our recent review dealing with pernicious anaemia (PRESCRIBER, 1936, Feb , 60) the work of Dakin and West (New York) in separating the active haematopoietic principle of liver was described Since then this principle—a polypeptide—has been produced commercially in this country under the name of *Anahaemin* (British Drug Houses), and is supplied in ampoules containing 100 mg per c cm , average dose 200 mg injected monthly

Quite recently GREENSPON (Montreal) has described a series of experiments which throw doubt on Castle's hypothesis of an 'extrinsic factor' He shows that pepsin is antagonistic to the antianaemic factor in the stomach, and he suggests that Castle's intrinsic factor may be a precursor of the haematopoietic principle of the liver, which may be a hormone, or alternatively that the stomach factor is a kinase through the action of which the active liver principle is formed

Some extracts of liver have been found to exercise a powerful effect in reducing the blood-pressure, but the factor causing this effect is little understood A principle called *Eutonon*, which has an effect on the heart muscle, has already been referred to

SHIBATA and colleagues (Tokohu Imperial Univ) are continuing their studies of *Yakriton* which they regard as the 'detoxicating hormone of the liver' They have studied its action on blood sedimentation, on leucocytosis, on the blood picture, on the hypoglycaemic action of insulin (which it counteracts), on the kidneys, on avitaminosis, and on the tubercle bacillus

The Pineal Body.—The pineal body or gland, known also as the epiphysis cerebri or conarium (the names 'pineal' and 'conarium' from its shape like a pine cone), is a small, pinkish cone shaped structure about the size of a pea, resting on the anterior corpora quadrigemina and connected with the third ventricle It measures about 8 mm (⅓ inch) in length and is attached at its base by a stalk Of its functions very little is known For a long time it was believed to be the vestige of a median eye Whether or not it produces an internal secretion is not known Recent work points to some relationship between it and the anterior pituitary

ROWNTREE, CLARK, STEINBERG, and HANSON (Philadelphia), whose work on the thymus was recorded last year, now report experiments with extracts of the pineal gland The extract (an aqueous acid derivative, probably a picrate) was injected into succeeding generations of parent rats and was found to hasten the onset of adolescence in the offspring The end result was dwarfism with precocious development and macrogenitalism, and these effects were amplified in succeeding generations

ENGEL (Vienna) has studied the effect of pineal extract on sexual development, the sex hormones, and the gonadotropic hormones of the anterior pituitary He finds it has an inhibiting effect on both gonadotropic pituitary hormones, the follicle-stimulating (prolan A)

and the luteinizing (prolan B) principles This property is shown by alkaline extracts

HOFFSTÄTTER (Vienna) has treated over 150 cases of sexual 'hyperlibido' with an extract of pineal gland In 90 cases the result was good, in 22 improvement was partial, while in the remainder it had no effect

The Stomach, Duodenum, and Intestines.—The successful use of desiccated stomach in the treatment of pernicious anaemia points to the presence in stomach membrane of an antianaemic factor This principle, which is believed not to be a hormone, is dealt with in the paragraph on the Liver

The Duodenum—In 1902 Bayliss and Starling discovered that an acid extract of duodenal mucosa, when injected intravenously, provoked profuse pancreatic secretion The active substance of this extract they called *Secretine*, concluding that it was an internal secretion Their work has since been fully confirmed, though the exact composition of secretine has not yet been established Secretine is occasionally employed therapeutically as a stimulant to the pancreatic external secretion when this is deficient According to IVY (Chicago) secretine has no therapeutic value, it is ineffective when taken by mouth, and it is relatively inactive hypodermically

The Intestines—Ivy, in 1928, found that an extract of the upper intestinal mucosa caused contraction and evacuation of the gall-bladder, and suggested the name *Cholecystokinin* for the chemical substance responsible for this effect It is closely allied to secretine but is probably not identical with it Given intravenously it acts on the gall bladder in the manner described, but it is not superior to other agents for this purpose

The Thymus.—The general opinion to day is against the inclusion of the thymus among the endocrine organs Until lately it was so regarded because observers had described certain changes as a result of its removal Recent work, however, has demonstrated that extirpation of the thymus produces no appreciable result An investigation on the so-called 'status thymico lymphaticus,' made on behalf of the Medical Research Council, shows that this condition does not exist as a pathological entity

The literature on the thymus is still fairly voluminous, but the conclusions offered regarding its endocrine nature are indefinite ROWNTREE (Philadelphia) suggests a relationship between the thymus and the parathyroids, the glands appearing to be associated in development and to have functions in common The most interesting results are those of ROWNTREE, CLARK, and HANSON, whose previous work was recorded last year According to them, continuous administration of thymus extract to successive generations of animals was followed by remarkable acceleration in the rate of growth of the offspring as well as in the onset of adolescence The difference in the appearance of the fourth and fifth generation of rats

continuously treated was most striking These workers are now studying the effect of thymus extract clinically and the work is still in progress

Minor Organs —Certain minor organs appear from time to time in the literature with the suggestion of a possible endocrine function

The Salivary Glands —While there is no evidence indicating the secretion of a hormone by the salivary glands recent work by WEISMAN and YERBURY (New York) is of interest The close relationship of the salivary secretion to the blood stream suggested that the anterior pituitary like hormones found in the urine might also be found in the saliva but careful testing by the Aschheim Zondek method and by the vaginal smear test showed that the saliva contains no such hormones

The Kidneys —From time to time something appears in the literature suggesting an endocrine action of the kidneys During the past year GOMEZ has reported the action of extracts of kidney cortex on urea retention Most patients showed a decrease in blood urea some showed an increase and others no change JABLONS reports encouraging results with kidney extracts in the treatment of hypertension but his results have not been confirmed

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COMMON MALADIES AND THEIR TREATMENT.

XXXV. Morbidity Associated with Menstruation.

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THE minor degrees of disability associated with menstruation probably cause more trouble and invalidism than the graver lesions which come to the gynaecological specialist. Not only are the very serious conditions of less frequent occurrence, but when they do appear patient and practitioner alike recognize the necessity for prompt action, whereas women will go on bearing the smaller miseries which the menstrual cycle can bring in its regular, or irregular, course with a stoicism worthy of a better cause.

The main reason for this misplaced fortitude is no doubt a deeply rooted belief that menstruation is so near akin to an incurable illness that any suffering or disability associated with it is normal, or at any rate inevitable. There is much to support this view of a function which is physiological, for when it does merge into or become associated with a pathological condition treatment is difficult and the results are often disappointing.

That menstruation is a natural process which should fulfil its function without causing ill-health or undue inconvenience needs to be better appreciated if a higher standard of sexual health is to be obtained, and no one is more fitted to enlighten his patients on these matters than the family physician. By obtaining their confidence and letting them feel the importance he attaches to a smoothly running monthly period he will get them to consult him at

the earliest indication of anything not quite up to the standard of well-being which he has put before them.

An important part of this branch of preventive medicine is to advise those in charge of his child patients who are approaching puberty that girls should be warned what to expect, reassured, and instructed in the personal hygiene and general management of the period. If not prepared, children and young girls may get a severe shock when they see what, to them, is a severe haemorrhage. This coming at a time of life when the nervous system is unstable can cause considerable general and emotional upset.

At first a girl is apt to be irritable, nervous, and depressed at the periods, and may find it difficult to adjust herself to the change in her life. Here the physician can help her by explaining to the mother, schoolmistress, or whoever has the care of the child something of the changes and developments which are taking place in mind and body, and advising sympathy and forbearance while the newly acquired functions are becoming established. At the same time he has the opportunity of urging that the girl should be led to understand that the occurrence is the normal sequence of growth and must be so accepted, and not looked upon as a grievance or an ever recurring invalidism.

For the first few months irregularity in time and amount of discharge need not be regarded as morbid. If it persists, however, investigation as to the cause and the institution of treatment are imperative. The condition indicates faulty hygiene, such as insufficient exercise, overwork, excess in games, lack of sunlight and fresh air, food deficiency either in quantity or quality, late going to bed, etc. Or some constitutional disease may be the underlying cause, for example early tubercle or anaemia. It is not always recognized that endocrine dysfunction leads to various disturbances of the menstrual cycle not only at puberty but throughout the years of sexual activity. It is important that any menstrual irregularity should be treated in the early stages even if it is not in itself an apparent cause of trouble, for it is an indication of some constitutional upset which if not corrected will tend to get worse. Also a normal menstrual function is of great economic importance to girls and women engaged in salaried employment, for if a day or two of 'sick leave' is required every three or four weeks women can scarcely expect to draw equal pay with their male co-workers.

Premature onset of menstruation involves certain difficulties, as the child's physical precocity has outstripped her true mental and intellectual development. She may be much upset by what is a real drawback at her time of life amongst the companions of her own age. It falls to the physician to see that the mother and schoolmistress realize this and give her the care and supervision she will need. Other signs of precocious sexual development must be watched for, and such guidance and teaching given as may be necessary.

Delayed Onset.—If the onset of menstruation lags much beyond the average time, say after fifteen and a half, investigation is called for, as it points to delay in development, subnormal health, or a local malformation such as imperforate hymen.

It is noticeable in practice that women of the asthenic type, lacking in energy and enterprise and generally below par, often give a history of having begun to menstruate at sixteen or seventeen years or later, and seeing them one wonders whether they might not have enjoyed robust health had the sexual retardment been recognized and treated medically at the age of puberty. Rectification of any unhygienic conditions in the home, school, or place of work is required. Also the diagnosis and treatment of chronic disease apart from the sexual system is necessary. Further, as menstruation is controlled by the endocrine glands it can be accepted as certain that they are at fault, either primarily or secondarily to some toxic or other cause. One or other may be the dominating factor, or the normal balance between the anterior pituitary, ovarian follicular hormone, and the corpus luteum may be upset. The important rôle of the thyroid, with its physiological enlargement at puberty and during pregnancy, must be borne in mind in arranging a course of treatment for any case of abnormal menstruation.

Imperforate Hymen is sufficiently common to be remembered as a possible cause of the non-appearance of the menses. Cramp-like pains in the lower abdomen recurring at regular intervals of three or four weeks with perhaps some swelling above the pubis which tends to increase in size, a general toxic appearance, and a history of absolute amenorrhoea are sufficiently suggestive signs and symptoms to call for a local examination.

At any age the physiological cause of amenorrhoea must be considered. That pregnancy can occur before the establishment of menstruation is a well authenticated fact.

Morbid menstruation in adult women may be due to the same causes as in the adolescent girl and will then require a similar scheme of treatment. But the older patients are liable to suffer from conditions which are less frequently found in young girls. Malignant and benign new growths, syphilis and gonorrhoea, trauma following parturition, and retained products of conception may be mentioned in this connexion.

Severe headaches at menstruation suggest anterior pituitary origin, as does menorrhagia if other obvious causes are absent.

Middle-aged women are too prone to attribute to the menopause all ill-health in any way connected with menstrual function, and instead of seeking treatment they will rely on the course of nature to cure what may be a serious pathological condition. Profuse or irregular haemorrhage from a uterine fibroid or a cervical polypus may exsanguinate a woman before she is brought to realize that she is suffering from a curable complaint and not from a physiological process of involution.

The menopause is an epoch when the family physician can do much to help his patients both by warning them against these false ideas of the cause of illness at this time of life, and by judicious management of the discomforts and morbidity which are apt in varying degrees to accompany the change.

Administration of Iron.—LUCAS and HENDERSON (Univ. of Toronto) are of opinion that ferrous chloride surpasses all other forms of iron in the treatment of anaemia From 2·5 to 7·5 grains *of this salt (equivalent to 1-3 grains of iron) is equal in effect to* 6-10 grains of ferrous sulphate, 30-50 grains of reduced iron, 60-90 grains of iron and ammonium citrate, or the same amount of Blaud's pill Iron given by intramuscular injection is almost valueless [The form of ferrous chloride recommended is the Syrupus Ferri Chloridi of the Canadian formulary, which contains about half a grain (32 mg) of ferrous iron in each drachm. It is prepared by digesting reduced iron in hydrochloric acid and adding syrup.]

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RECENT WORK ON ANTISEPTICS

An Abstract Review.

THE definition of an antiseptic given by Browning and quoted in our review last year (PRESCRIBER, 1935, June, 208) is 'a substance of ascertained chemical composition harmful to the activities of micro-organisms' This covers both classes of antiseptics—bactericides, which kill bacteria, and bacteriostats, which simply prevent their growth and multiplication In assessing the value of an antiseptic its selective action on different bacteria must be considered, as also its relative harmlessness to the human organism A proper appreciation of the value and limitations of antiseptics has led to much research during recent years, especially in relation to the influence of chemical constitution on bactericidal properties

Some interesting results are given by WOODWARD, KINGERY, and WILLIAMS (Univ of Oregon), who have compared the fungicidal action of three phenol derivatives on *Monilia tropicalis* with other antiseptics in the presence of blood serum, vesicle fluid, and hide powder It was found that the fungicidal power of iodine was greatly reduced by serum, vesicle fluid, and hide powder, that of n hexylresorcinol was reduced but the diminution was less than that of iodine, chlorothymol failed to kill in the presence of proteins, while thymol was effective only in the presence of hide powder, benzoic acid, salicylic acid, and sodium thiosulphate were entirely ineffective in the protein suspensions, but sodium hypochlorite maintained its killing power in high concentrations They conclude that the higher phenols are worthy of further clinical study in the treatment of fungus diseases, but that a drug more specific in its action is still needed

Dealing with the preparation of sterile solutions, DAVIS (London) reports a careful study of the tyndallization process recommended by the British Pharmacopoeia for the sterilization of solutions for injection In this process the solution is distributed in the final containers (ampoules, etc) which are then sealed and heated to 80° C for one hour on three successive days Davis finds that in the presence of contaminating spores a sterile product is not obtained by this process, whereas in the absence of spores, and with suitable precautions in regard to cleanliness and sterility of containers, ordinary injection solutions are sterile after the first heating The process of tyndallization, Davis says, will have to be considerably modified if it is to be retained officially

Skin Disinfection—A simple formula for a mercuric chloride solution for skin disinfection is offered by VAICHULIS and ARNOLD as follows Mercuric chloride 1 0 gm , hydrochloric acid 10 c cm , chrysoidin-Y 2 0 gm , alcohol (95 per cent) 600 c cm , acetone 200 c cm , water to 1 litre This solution has a high phenol coefficient,

it penetrates the skin and removes fat, it does not irritate, and the colour disappears from the skin within twenty-four hours It gave efficient sterilization in nearly 500 cases (See also Mercurials)

Acridine Compounds—Of the acridine compounds in use, *Acriflavine*, B P (Acriflavine Hydrochloride, U S P 1936) or 2 8 diamino-10 methylacridinium chloride hydrochloride, is the best known *Euflavine*, or neutral acriflavine (Acriflavine, U S P 1936), is acriflavine less a molecule of hydrochloric acid, it is preferred in some cases as being less acid *Proflavine* is 2 8 diaminoacridinium sulphate, it is specially suited for use in ophthalmic work *Trypaflavine* is the original German name for acriflavine, the name is no longer used in this country The word 'flavine' should not be used in connexion with these dyes, as it is the name of a vegetable colouring matter

The value of acriflavine as a urinary antiseptic is discussed by ASSINDER (Birmingham) As a routine in cases of acute gonorrhoea he gives intravenous injections of 2 to 4 c cm of a 2 per cent solution in sterile distilled water Ten such injections constitute a course In nearly 5000 cases he has found it shorten the duration of the discharge If the posterior urethra is affected it helps to clear the cystitis, if it is not affected acriflavine apparently protects it In *B coli* infection of the urinary tract similar treatment gives results which compare very favourably with those obtained by the use of ketogenic diet or mandelic acid For nearly five years the tolerance of the patients to acriflavine was generally good A few cases of dermatitis occurred and an occasional case of toxic jaundice, but more recently jaundice began to occur with great frequency For the past twelve months Assinder has been using a non toxic product, acriflavine intravenous' (British Drug Houses), this has been used in 300 cases with only two cases of transient liver damage Before each injection the urine is examined for urobilinogen this is now conspicuously absent, whereas with the former product it was found with great regularity

The difficulty in preparing an elegant and suitable emulsion of acriflavine for use in the treatment of burns, abscesses etc, has long been felt, the formulae given in textbooks usually being complicated and time consuming TOMB (Cairo) offers a very simple formula for the rapid preparation of a 1 1000 emulsion Acriflavine, 1 gm, is dissolved in lime water, 500 ml, then 500 ml of arachis or olive oil is added and the whole shaken thoroughly TRILLWOOD (London) suggests a slightly different formula acriflavine, 1 gm, is dissolved in 100 ml of water, olive oil, oleic acid, and saccharated solution of lime are triturated with this to form a cream, and olive oil or liquid paraffin is then added to make one litre Either formula gives a good emulsion and both are simple in working Tomb's process is somewhat more rapid in execution

Mercurial Antiseptics.—The more important mercurial antiseptics at present in use are *Mercurochrome*, *Metaphen*, *Merthiolate*, and *Phenylmercuric Nitrate*.

Mercurochrome.—This mercurial dye is the disodium salt of 2 : 7-dibromo-4-hydroxymercurifluorescein and contains 24-26 per cent. of mercury. Its full name is 'mercurochrome-220 soluble,' and it occurs as iridescent green scales or granules, freely soluble in water. It is practically insoluble in alcohol; the minute trace dissolved colours the liquid pink, but the solution is much too weak to be of use. It is incompatible with acids, which precipitate an insoluble mercury compound; it is also precipitated by cocaine, by procaine, and by almost all the local anaesthetics.

The action of mercurochrome and of iodine on normal skin and in infected wounds has been investigated by HILL (Johns Hopkins Hospital). He shows that under conditions of practice no antiseptic can invariably sterilize heavily infected skin. Aqueous solutions of antiseptics are not as a rule suitable for preoperative skin sterilization. Both aqueous solution (2 per cent.) and tincture of mercurochrome (2 per cent. in water 35, alcohol 55, and acetone 10) are bactericidal and bacteriostatic on human skin, but the tincture is superior to the aqueous solution. In order of efficacy mercurochrome tincture comes first, then 7 per cent. tincture of iodine not removed with alcohol; after these 2 per cent. aqueous mercurochrome, and lastly 7 per cent. tincture of iodine, removed with alcohol. For heavily infected wounds aqueous mercurochrome is superior to the tincture and to iodine; it keeps the bacterial count lower and does not interfere with phagocytosis.

The use of mercurochrome to effect vaginal antisepsis during labour is advocated by MAYES (Brooklyn, N.Y.). In 6000 cases only one patient in a thousand had a morbidity lasting twenty days. No injurious effects on mother or child were observed, the only drawback to its use being its staining property. A 4 per cent. aqueous solution was used to spray the perineum, except at time of delivery, when a 4 per cent. aqueous-acetone solution was used. Three drachms of the aqueous solution was first of all instilled into the vagina by a syringe, and this was repeated every twelve hours during labour.

Metaphen is the subject of a special article appearing elsewhere in this issue.

Merthiolate is sodium ethoxymercury thiosalicylate, and contains 49 to 50 per cent. of mercury in organic combination. It is a cream-coloured crystalline powder, soluble in water and in alcohol. It is much less toxic than mercuric chloride and does not precipitate serum-protein. Its special application is surface sterilization, an isotonic solution 1 : 1000 being used for general application, while for sensitive mucous membranes a weaker solution (1 : 2000 to 1 : 5000) is recommended.

DAVIS (London) has studied the germicidal action on *Staphylococcus aureus* of some common antiseptics, and he finds that merthiolate is by far the most powerful germicide, a solution 1 100,000 being sufficient to kill this organism within thirty minutes As its solutions are alkaline it cannot be used as a preservative for hypodermic solutions, but it is a useful preservative for serums and vaccines and is preferable to phenol or trikresol

Phenylmercuric Nitrate, $C_6H_5HgNO_3$, is a crystalline substance only slightly soluble (about 1 850) in water Phenylmercuric chloride, C_6H_5HgCl, is also crystalline and is still less soluble (about 1 20,000) in water The preparations recommended are (1) a solution of phenylmercuric nitrate, 1 1200, in a mixture of water 90 per cent and diethyleneglycol 10 per cent by weight, (2) a solution of the same salt, one part in 99 parts of diethyleneglycol by weight, (3) a solution of the same salt in glycerin, 0 01 per cent by weight, (4) an ointment containing phenylmercuric nitrate one part in 1500 by weight in an oxycholesterin base, (5) a jelly containing one part of phenylmercuric nitrate in 1500 parts by weight of a mixture of gum tragacanth, glycerin, and water, (6) phenylmercuric chloride, 1 30 000, in 0 85 per cent solution of sodium chloride

BISKIND (Cleveland, Ohio), discussing generally the therapeutic application of phenylmercuric salts, makes special reference to their use in gynaecology He has used an aqueous solution (1 1500) of basic phenylmercuric nitrate in some hundreds of cases with excellent results, the cases including vaginitis, trichomonas infection, endocervicitis, paracervical sinus, retrovaginal fistula, postoperative slough, and tinea cruris The solution is instilled into the vagina by means of a syringe, or diluted about 1 250 for use as a douche It is odourless, non irritant, non corrosive to instruments, and quite stable In tinea cruris the ointment was used

Urinary Antiseptics —Reviewing generally the subject of urinary antiseptics, TAIT (Melbourne) emphasizes the necessity for exact diagnosis before selection of the antiseptic The form of chronic urinary infection most frequently met with—chronic pyelitis and cystitis—presents most difficulties In all other infections a reliable treatment is well defined, but when invasion by one of the coliform group of organisms is well established and recurrently maintained the condition is notoriously resistant to treatment and the search for a curative urinary antiseptic is likely to be prolonged Hexamine is the most generally useful antiseptic, pyridine and neotropin are of value, hexylresorcinol, while effective, has certain disadvantages Results will be improved by controlling the source of infection, by building up the natural bactericidal powers of the body, and by ensuring a free flow of urine in an antiseptic fluid throughout all parts of the urinary tract

The use of mandelic acid to combat urinary infections was explained in our issue of September last (p 288) It is known that a

ketogenic (high fat) diet increases the acidity of the urine and prevents growth of bacilli by the formation of β-hydroxybutyric acid. This acid, being unstable, is unsuitable for administration, but mandelic acid, a nearly related compound, is excreted unchanged in the urine and renders it bacteriostatic. Mandelic acid is phenylhydroxyacetic acid, $C_6H_5.CHOH.COOH$: it is soluble in water and in the form of sodium salt is not unpalatable and does not irritate the stomach.

ROSENHEIM (London) was the first to report its use as a urinary antiseptic. He administered it in twelve cases, in doses of 3 gm. four times daily, neutralized with sodium bicarbonate, the acidity of the urine being maintained by ammonium chloride, which was given in eight 1 gm. doses during the day. His results were most gratifying. Rosenheim's experience is confirmed by LYON and DUNLOP (Edinburgh), who report sixteen cases in thirteen of which the treatment was successful in sterilizing the urine. Rosenheim's technique was employed, the drug being given in combination with sodium bicarbonate and accompanied by ammonium chloride. ALEXANDER (Teddington) reports a personal experience of its use in chronic cystitis, and adds: 'After I had spent a small fortune trying other remedies, sodium mandelate finally did the trick, and up to the present has given me a new lease of life.'

A further report by HOLLING and PLATT (Sheffield) describes treatment of twenty-nine cases, twenty-four of which showed sterile urine within periods varying from two to twenty-one days. Of the five failures three at least were unsuitable cases in which recovery was not anticipated. At first Rosenheim's method was followed; later the drug was given in the form of sodium mandelate, 50 grains four times daily with ammonium chloride, and finally four cases were treated with ammonium mandelate. With this salt it was found possible in most cases to dispense with the unpalatable ammonium chloride. A dose of 50 grains or less of ammonium mandelate is sufficient to bring the urinary *pH* to the necessary figure (5·3): if it fails to do so it may be supplemented by ammonium chloride.

CUBITT (London) points out that the real test of the efficiency of mandelic acid will be the duration of its sterilizing effects. Some cases relapse and will require renewed treatment in the form of a short course every month or so to keep them free of infection. Cases of uncomplicated *B. coli* infection are undoubtedly the most favourable for treatment; cases of mixed infection are only slightly, if at all, benefited, but Cubitt reports five cases with secondary organisms (staphylococcus and streptococcus) two of which were distinctly improved, and he thinks that mandelic acid should receive a trial in such cases. He has found great variation in the amount of ammonium chloride required to keep the urine at a *pH* of 5 to 5·3.

A case treated with mandelic acid is recorded by CHAPLIN (London) in which toxic symptoms developed on the tenth day of treatment. Severe aching of the muscles of the neck and leg, with urticarial rash,

occurred after each dose and increased in intensity during several days Treatment was stopped and no further attacks took place There was definite improvement in the bladder condition Chaplin suggests that as mandelic acid is allied to lactic acid, it may produce an artificial muscle exhaustion in a susceptible person

Mandelic acid and sodium mandelate are commercial products Ammonium mandelate, being hygroscopic, is issued in the form of an elixir, *Mandelix* (British Drug Houses), containing in a 2 drachm dose the equivalent of 45 grains of mandelic acid A preparation called *Neobet* (Boots) is in the form of granules consisting of mandelic acid, sodium bicarbonate, sodium acid phosphate, and flavouring The sodium acid phosphate maintains the acidity of the urine and takes the place of ammonium chloride The dose is two teaspoonfuls, representing 45 grains (3 gm) of mandelic acid

The use of acriflavine as a urinary antiseptic is mentioned under Acriflavine

Miscellaneous —The antiseptic action of *urea* has been investigated by FOULGER and FOSHAY (Cincinnati) Cultural experiments showed that *B coli* and other organisms were killed rapidly *Staphylococcus aureus* was particularly resistant to urea, surviving after twenty four hours exposure *S albus* survived for four hours only Tested clinically it proved useful in cases of purulent otitis media a fresh saturated aqueous solution of urea being instilled into the ear every four hours In a severe streptococcic throat infection in a girl aged 5, where other treatment had failed and the child appeared moribund irrigation with urea solution cleared up the foul discharge Unfortunately the patient died a week later from peritonitis

Azochloramid —As mentioned in last year s review, this new antiseptic was recently introduced in America as suitable for dental practice Its composition is N-N dichloroazodicarbonamidine, $NH_2(NCl)$ CN NC $(NCl)NH_2$ the chlorine being attached to a nitrogen atom as in the chloramines It contains 38 8 per cent of active chlorine, which is liberated slowly in presence of organic matter The rate of liberation of chlorine is much slower than in the case of hypochlorite or chloramine Azochloramid occurs in yellow crystals, odourless and tasteless, and soluble in water, lipoids, and most organic solvents In therapeutic concentrations it is non-toxic and non irritating It is used in the sterilization of dental pulp canals and periapical abscesses in the treatment of fistulas, and as a wet dressing for infected wounds It is ineffective when administered internally or intravenously A solution in triacetin (glycerol triacetate) 1 100 is used for root canal treatment, and a similar solution 1 500 for dressing and packing wounds

KENNEDY (New York) reports its use in over 100 cases of infected wounds As a wet dressing or irrigation he recommends a solution 1 3300 in normal saline solution, and for local application on gauze

the 1 · 500 solution in triacetin He suggests its use in unclosed lacerated wounds, as a prophylactic in compound fractures and in abdominal operations, in abscesses of all types except when foreign bodies are present, in preparation of burnt areas for skin grafting, and as a continuous wet dressing over fresh pinch grafts

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Whooping-Cough. Nembutal.—R JARMAN reports that a suppository containing 1 grain of nembutal gives the child a perfect night's rest with complete relief from coughing—*B.M J*, Feb 1, '36, p 236

Ammonium Acid Phosphate.—According to S ALSTEAD (Glasgow), ammonium acid phosphate is much superior to the sodium salt as an acidifier of the urine. In doses of 2 0 gm thrice daily it markedly diminishes the *p*H of the urine, and this never falls below 4 7 to 5 5 even with large doses Its saline cathartic action is not manifest except with very large doses—*Edinburgh Med J*, May '36, p 292

BAUKE (Frankfort on-Main) records his observations on forty-six patients *suffering from peptic ulcers* The most suitable case is the recent florid type at its acute form during the crisis, the recurring ulcer is less amenable to treatment In gastric ulcer a cure may be achieved with 18-20 injections, in duodenal ulcer up to 25 injections may be necessary If the cases are properly selected the final results are uniformly good

BOGENDÖRFER reports thirty cases in which the results in many cases are described as 'amazing' The diagnosis was always clear and no other treatment was given

KÖNING (The Hague) states that it afforded relief in two post operative cases in which peptic ulcer was suspected

STOLZ and WEISS (Strasbourg) record sixty cases of gastric and duodenal ulcer treated during 1934-35 Forty-two patients were treated with histidine (larostidin) injections only, the remaining eighteen were surgical cases and histidine was used prophylactically to prevent relapse Good results were obtained in thirty-seven cases, fair results in two, and negative results in three

MANGINELLI (Rome) reports fifty one observations, from which he concludes that histidine has a rapid and intense analgesic effect in gastro duodenal ulceration, vomiting ceases and food is better tolerated Its curative action is specific Its analgesic action is of service also in gastric neuroses and in cholecystitis In malignant tumours and in colitis the results were less satisfactory

FROMMEL, HERSCHBERG, and TROTTET (Geneva Univ) report animal experiments to determine the action of histidine on the cardiovascular system They find that it has no harmful action on the heart, and that even in large doses no fear need be entertained of heart failure No signs of intolerance were observed after administration of very large doses

ALSBERG (Hamburg) reports fourteen cases treated successfully In some cases he gave injections only twice or three times a week instead of daily, and with equally good results

KORBSCH (Berlin), in a lengthy report, emphasizes the point that histidine must not be expected to make good every deficiency connected with peptic ulceration

With so large a number of favourable reports there can be no doubt that histidine is a remedy of great promise It should be noted that almost every observer records a small percentage of failures, a fact that points to certain limitations in its use like all remedies it must be used only in properly selected cases Still no record appears of its ever doing harm, and as the chances are at least 75 per cent in its favour there is no reason why histidine should not receive a trial in all cases of peptic ulcer

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New Drugs and Preparations.

[Under this heading are given brief notices of new non secret products as they appear on the market or are mentioned in medical literature The notes are intended for reference only, and must not be taken to imply anything in the nature of a recommendation In most cases the information is derived wholly or mainly from makers' advertisements]

A.B.D. Capsules.—Contain vitamins A, B_1, B_2, and D, each representing 3 teaspoonfuls cod liver oil, and 1¼ ounce yeast, or 6200 vitamin A units, 900 vitamin D units, 45 Sherman units vitamin B_1, and 10 S U of vitamin B_2 Dose, 1 to 3 capsules daily (Abbott Labs, London)

Acaprin—A synthetic urea compound of the quinoline series, recommended by Hörlein (Elberfeld) as an effective remedy for piroplasmosis—*Proc Roy Soc Med*, 1936, Feb, 313-324

Adsperlen—A liquid preparation containing extract of adrenal cortex with spleen and thyroid Dose, 10 drops thrice daily by mouth, combats infection and raises low blood pressure rapidly (Endocrines Ltd, Watford)

Anahaemin.—The principle of liver active in pernicious anaemia, as isolated recently by Dakin and West Ampoules sterile solution, 0 1 gm per c cm Dose, 2 c cm intramuscularly, once a month, in extreme cases larger doses at shorter intervals (British Drug Houses, London)

preparation and action, and its possible substitutes Complete bibliographies are given and a good index is appended The get up of the book shows a tendency towards 'modernism' that is hardly suited to a scientific work—for example the word 'Insulin' appears vertically on the back like a sign of the Underground Railway, and the chapter headings appear between formidable black lines like mourning borders These, however, are small matters the book will be most useful for reference and should see many editions T S

Glandular Physiology and Therapy A Symposium Prepared under the Auspices of the Council on Pharmacy and Chemistry of the American Medical Association Pp 528 (Amer Med Assoc, Chicago $2 50)

During the past twelve months or so a series of articles dealing in turn with the various endocrine glands appeared in the pages of the *Journal of the American Medical Association* These articles were by acknowledged experts they summarized the state of knowledge at the time of writing and they were characterized by a careful conservatism which gave them a special value Following publication of these articles in the Association's journal, an opportunity was given to the authors of revision and the series has now been issued in book form It contains thirty one chapters of these ten are devoted to the pituitary, eight to the gonads, two to the adrenals five to the thyroid and parathyroids, two to the pancreas and insulin and four to other endocrine glands and their products References to the literature appear at the foot of each page and a well arranged index at the end permits of ready reference

The rapid development of endocrinology and its immense importance to medicine make a work of this sort particularly welcome The only drawback is the continued rapid advance of knowledge, as hardly a month passes without some announcement of significance, but the Association promises a new edition as soon as developments render this necessary Meanwhile this book, which is well printed on good paper and neatly bound in limp roan, should fill a place in the physician's library as an up-to-date reference book on endocrine therapy T S

Muscular Exercise By M Grace Eggleton, M R C S, L R C P, M Sc, Department of Physiology, University of Edinburgh Pp 298 (Kegan Paul 10s 6d)

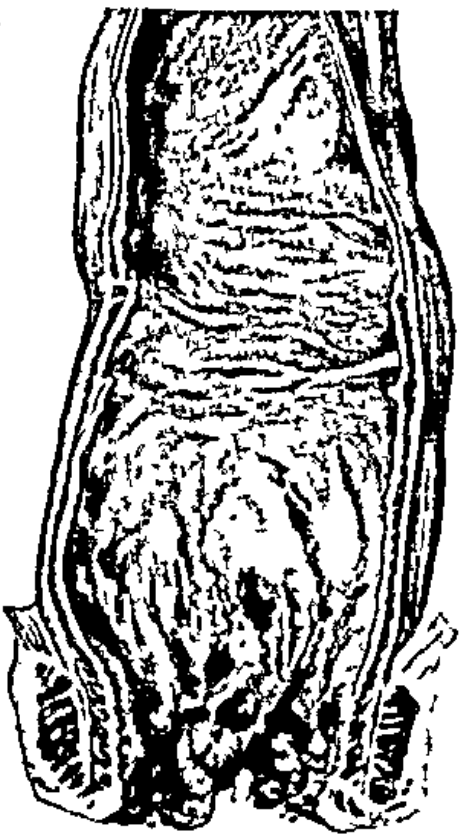
In the preface to this book the author tells us that her object has been to help to dispel the atmosphere of magic and mystery that still surrounds the human body The book is addressed to that rather large class known as 'the intelligent lay reader,' and the author endeavours to show, as far as possible in non technical language, just what happens in the various parts of the body when the muscles are in motion As muscular exercise affects the respiration, the circulation, the metabolism, the acidity, the body temperature, the nervous system, and the endocrine activity, it will be seen that under a short title our author covers a large field The book is full of information interesting to the ordinary reader there is much about blood pressure, for example, and the emergency action of adrenaline is lucidly explained Why persons faint on long standing and why a fat person gets hot sooner than a thin person on the same amount of work, are among the many questions answered The final chapter is devoted to the question of athletics

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The combined use of ointment and suppositories is recommended in cases exhibiting much external irritation and inflammation Case reports and Free Trial Supply will be sent on application to Chas Zimmermann & Co. Ltd., 9-10 St Mary-at-Hill, London, E.C. 3. Tel. Mansion House 6005.

Hydrotherapy and Climatotherapy By Matthew B Ray, D S O, M D, M R C P Pp 312 (Ed Arnold 12s 6d)

Dr Ray is not only one of our leading authorities on rheumatism, but he is well versed in hydrotherapeutic measures and has an intimate acquaintance with the spas, British and foreign Of the two parts into which this book is divided, the first deals with baths, waters, and spa treatment and the second with climate and climatic resorts As was pointed out in our recent Spa Number, the choice of a spa is to a great extent a question of climate Here the climates of British and foreign resorts are succinctly described and the indications for the different climates are discussed The spas are grouped according to the class of disorders for which they are best suited The book is an excellent summary of the whole subject and should serve the practitioner well as a work of reference

T S

A Synopsis of Surgical Anatomy By Alexander Lee M'Gregor, F R C S Eng Pp 664. (Wright, Bristol 17s 6d)

The third edition of this excellent Synopsis appears only eighteen months after its predecessor It has been revised and amplified by a dozen new figures, making 648 in all A more detailed account is given of the thyroid gland and its nerves, and of diaphragmatic hernia These increases with each edition will doubtless in time make the work more complete, although it already presents the more essentially practical points of anatomy in more or less separate essays, so that the book need not be read from the beginning to be understood It is beautifully reproduced and should be of very definite value to the student and practitioner for whom it is intended

W M

Synthetic Anatomy By J E Cheesman Complete in fourteen parts (Baillière, Tindall & Cox 3s per part, postage 2d Complete work in binding case, 45s)

This work may be described as unique It is not exactly a book, but a binder containing a number of separate atlases, each representing a portion of the human body and consisting of a number of superimposed transparent coloured plates Taken together these plates represent depth, taken singly they depict sections A descriptive index accompanies each atlas and is so arranged that it lies open on both sides of the plate with a blank white sheet to go below the transparency or transparencies being studied By means of 'map references' and a side scale (like a geographical atlas) any part or organ can readily be found and examined The plates being printed on transparent tissue can be examined either singly or several at once, and in this way a picture of any part of the body can be obtained with ease The complete work comprises fourteen parts, two of which (9 and 9a) bear the same number Part 13 (the Eye and Orbit) which has only recently been published, completes the work

To students the atlas will of course be most helpful, especially in supplementing the work of the dissecting room by home study The practitioner also, who may at various times desire to refresh his memory on some point or other, is certain to find this clever production of great service

A new edition (thirteenth) of Mr H Wippell Gadd's SYNOPSIS OF THE BRITISH PHARMACOPOEIA, 1932, has appeared (Baillière, Tindall & Cox, 3s) This useful little pocket companion contains, in addition to a tabular arrangement of the contents of the B P, a useful digest of the laws concerning poisons and dangerous drugs, embodying the latest regulations

A new edition of FOOD, HEALTH, VITAMINS by Professor R H A Plimmer and Violet G Plimmer (Longmans Green, 3s 6d), has appeared, the seventh in ten years, which says much for its popularity In a rapidly advancing subject such as that of vitamins constant revision is necessary, and this has been done with such thoroughness that the book is an up-to date survey of the whole question of nutrition The diagrams, coloured and plain, add to its value The busy practitioner would be well advised to provide himself with a copy, for it furnishes an authoritative account in small space and is easily read

In QUESTIONS OF OUR DAY (Lane 8s 6d), Mr Havelock Ellis has at last emerged from the derided revolutionary as the esteemed veteran and acknowledged authority on the psychology of sex Although he has exchanged letters and books with that other exponent of sex—Freud—it is doubtful if he has succeeded in pouring the new wine of psychoanalysis into the old bottle of a mind trained in pre-Freudian principles The essays in this volume are all short and are readable in the extreme, they deal with a variety of subjects of perennial interest, from faith, philosophy, and religion to pessimism, freedom, careers, parenthood, and sterilization The revolutionary of yesterday is the orthodox conversationalist of to day neither the science nor the politics not even the religion of this volume can be read as an offence by any one

The British Pharmacopoeia Commission has issued the COLLECTED REPORTS OF COMMITTEES on material prepared for an Addendum to the British Pharmacopoeia, 1932 The Report is No 9 of the series and is dated February 1936 Its object is to elicit comment and criticism from those interested and it is not to be regarded as an official announcement A considerable number of new drugs have been recommended for inclusion by the various committees Of these the Clinical Committee has selected the following and recommends their inclusion in the Addendum to be issued during the present year Acetarsol ('stovarsol'), Argentoproteinum (protargol'), Bismuthi et Sodii Tartras, Calcii Chloridum Hydratum (for injection), Chiniofonum (yatren), Extractum Stramonii Liquidum, Extractum Stramonii Siccum, Ferri Subchloridum Citratum, *Histaminae Phosphas Acidus*, *Injectio* Bismuthi Oxychloridi, Liquor Iodi Aquosus (Lugol's solution), Oleum Iodisatum, Sodii Thiosulphas, Tinctura Stramonii, Tryparsamidum To this list are added Antitoxinum Oedematiens (gas gangrene), A Staphylococcicum, A Vibriosepticum, Serum Antipneumococcicum Types I and II, Acidum Ascorbicum (vitamin C), Calciferol (vitamin D), Liquor Calciferolis, Pulvis Vitamin B (an adsorbate upon fuller's earth) Several other drugs are mentioned but are not recommended by the Clinical Committee for inclusion—among these are calcium gluconate and ergometrine A considerable portion of the Report is devoted to technical details regarding standards tests, etc. The Report is obtainable at the office of the General Medical Council, 44 Hallam Street, London, W 1, price 2s 6d

THE MEDICAL ANNUAL, 1936 (Wright & Sons, 20s.), is the fifty-fourth issue of this useful volume and shows no sign of age. It fulfils as in former years all the functions of a year-book, and under the able editorship of Dr Letheby Tidy and Dr Rendle Short it well maintains the standard attained by previous issues. The various subjects are dealt with by nearly forty contributors, each an acknowledged authority in his own department. The illustrations are as usual a feature of the work, and the whole get-up is a credit to the publishers.

THE SECOND OLDEST PROFESSION, by Ben L. Reitman (Constable, 8s. 6d.), is introduced by a preface from the pen of that notable old crusader Dr Harry Roberts. The book is eminently one for the physician interested in public health or in socio-political work. It leaves no doubt that the pimp's job, if second in age, is first in ignobility. The author is pessimistic regarding his elimination without a complete revolution of the economic basis of society. The book is to be recommended to all students of sociology, whether medical or lay.

SOVIET SCIENCE, by J. G. Crowther (Kegan Paul, 12s. 6d.), embodies the author's observations in Soviet Russia during half a dozen long visits. It is written with calm scientific candour and tells how the organization of scientific and technical research is more complete and more far-seeing than probably in any other country. It is not haphazard, as much of it is in this country and America, but is carefully planned, each part being related to the whole so far as is humanly possible. The scientist, we are told, ranks high in Russia, higher than the politician for example, which is only right and proper; he is well paid, which is more than can be said for our scientists. In the face of all this one may well ask what contribution has Soviet Russia made to science in general and to medical science in particular during the last ten years? The best scientific work still seems to be done in Great Britain and America, in spite of our haphazard methods; even Germany appears to have become crippled in this respect. Still Mr Crowther's book is thought-provoking and we ought to be able to learn something from it.

AN ANCIENT REMEDY AND ITS MODERN UTILITIES is the essential portion of the twenty-word title of a little book by C. J. Macalister, M.D. (Bale, Sons & Danielsson, 2s. 6d.). It deals with the common comfrey, *Symphytum officinale*, long known as a wound healer, hence its Latin name. Reported cases of the healing of tumours and rodent ulcer by application of a decoction of the root are mentioned, but except in one case of rodent ulcer the author was unsuccessful in repeating such cures. Chemical investigation of the plant revealed the presence of a crystalline substance allantoin, which was subsequently prepared synthetically from uric acid. The virtues of allantoin as a cell proliferant and its uses in the healing of sluggish ulcers, wounds, etc., are fully described in this book. Dr Macalister's early work on allantoin was described in THE PRESCRIBER twenty-four years ago (1912, Feb., 60; 1915, Aug., 166), and about that time allantoin was fairly widely used, but for some reason or other it did not appear to become popular. In this book the author, with the assistance of Dr A. W. Titherly, who deals with the chemistry of allantoin, brings the record to date and presents a good case for a revival of interest in this drug.

The REPORT OF THE PHYSICAL EDUCATION COMMITTEE of the British Medical Association is an interesting document, containing many important suggestions for the improvement of the physical efficiency of the nation It is obtainable from the offices of the B M A , price 6d

Under the title WORSE THAN SLAVERY, the Annual Report for 1935 of the British Empire Leprosy Relief Association has appeared Copies are obtainable from the office of the Association, 131 Baker Street, London, W 1

BRITISH HEALTH RESORTS SPA, SEASIDE, INLAND, is the title of the annual handbook issued by the British Health Resorts Association (Churchill, 1s) It is produced on lines very similar to those of last year's issue, and it is again edited by Dr Fortescue Fox The Minister of Health contributes a Foreword Not only the spas but also the coast and inland health resorts are described and illustrated, while a section is devoted to those of the British Empire overseas, Australia Canada, New Zealand, South Africa, and the British West Indies being included An account is given also of the work of the Association

The April issue of the ARCHIVES OF MEDICAL HYDROLOGY contains, among other interesting matter, a full programme of the Annual Meeting of the I S M H to be held in Austria from 10th to 16th October The opening ceremonies and first medical discussion will take place at Innsbruck, after which the party will proceed to Badgastein, Hofgastein, and Salzburg Excursions may be made to Vienna and Budapest after the meeting Receptions and banquets are promised by the local authorities at the various places visited, and interesting discussions on hydrological subjects will take place each day A party will be formed to leave London on 9th October , the anticipated cost of travel will be £10 to £11 plus an inclusive charge of 180 schillings (about £7) for accommodation, transport, etc., after arrival at Innsbruck Non members can join the party on payment of a fee of £1 Full particulars can be obtained from the General Secretary, International Society of Medical Hydrology, 109 Kingsway, London, W C 2

The Marmite Food Extract Company Ltd have issued an interesting brochure entitled MARMITE IN PREVENTIVE AND CURATIVE MEDICINE Marmite, as has been mentioned repeatedly in these pages, is an autolysed yeast extract, particularly rich in the vitamin B complex, which appears to be remarkably efficacious in certain types of anaemia, particularly in the tropics The booklet gives a full account of its uses in medicine It is supplied free to the profession

Hanovia Ltd , of Slough, the well known makers of actinotherapeutic apparatus, issue an interesting pamphlet entitled THE MOST VITALIZING OF ALL MEASURES, in which are given one hundred clinical references on the use of actinotherapy in general practice The conditions discussed are those connected with debility, metabolism, endocrine disorders respiration, circulation, skin affections, nervous troubles, tuberculosis , the use of different forms of radiation is also described, and to all the references chapter and verse are appended The book is sent free to those interested

An interesting pamphlet entitled ACRIFLAVINE BOOTS, ITS PROPERTIES AND USES, has been issued by Boots Pure Drug Co Ltd , Nottingham It deals with the use of the acridine antiseptics in medicine A brief historical survey is followed by an account of the bactericidal and chemical properties of acriflavine, euflavine (neutral acriflavine), and proflavine as manufactured by that firm Numerous indications for their use are given, together with extracts from case reports and a selected bibliography, while a separate leaflet issued with the booklet describes the use of acriflavine in gonorrhoea The booklet is issued free to the medical profession

The fifth edition of A PRESCRIBER'S LIST has appeared The book has no connexion with this journal it is a list of proprietary remedies issued free to the medical profession by Roberts & Co , 76 New Bond Street, London, W 1 The products are arranged alphabetically, with maker s name, composition, price, indications, and dose The list is fairly representative, but one notices with surprise the absence of the products of several very well-known firms The book will prove useful for reference, but the publishers would be well advised in future editions to reduce its bulk (over 320 pages), which can easily be effected by adoption of a more compact lay-out

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ORIGINAL COMMUNICATION.

The Lithium Salts of Antimony in Bilharzia Infection.

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IN a discussion which took place in 1928 before the Royal Society of Medicine on the special uses of antimony, J. A. Gunn suggested that the difficulty of obtaining the lithium salt of antimonyl-tartaric acid in crystalline form might explain why it had not come into therapeutic use; he quoted Fargher and Grey as stating that the antimony salts form a series in which the toxicity diminishes, while the solubility increases, in the order of potassium, ammonium, sodium, lithium.

Lithium antimony-thiomalate is very soluble and is stable unless exposed to light or a temperature above 80° C. The drug contains 16 per cent. of antimony metal and its low toxicity may be due partly to the presence of sulphur in the molecule. The preparation is known as *Anthiomaline* and it has been used in the treatment of lymphogranuloma inguinale, leishmaniasis, and other skin conditions for which antimony is indicated.

G. M. Findlay has directed attention to the low toxicity of lithium salts of antimony, and Sezary and Bolgert and others have used them with success in schistosomiasis, in which condition the slight diuretic property of lithium assists in expelling the degenerating ova.

Anthiomaline is supplied in a 6 per cent. solution, each 2 c.cm. ampoule containing 0·12 gm. of the active product, which is equivalent to 0·01 gm. of antimony metal per c.cm.

In Natal, children of twelve tolerate 0·5 c.cm. as an initial dose and 1·5 c.cm. as a repeated dose. Two c.cm. is a sufficiently large repeated dose for a child and 4 c.c. doses should not be exceeded with adults. Excessive

doses cause salivation or retching and should be avoided in Europeans, natives, or Indians during treatment.

Even though the maximum repeated dose contains less than half the amount of antimony metal contained in the maximum repeated dose of tartar emetic, its therapeutic effect would seem to be greater on bilharzia patients, to judge from the more rapid destruction of the escaping ova.

Treatment has sometimes been extended over six or seven weeks, but four injections may well be administered each week and a cure may sometimes be obtained in less than the month usually required with tartar emetic.

Though investigations have shown that anthiomaline is easily eliminated from the body, this is no reason against injecting the drug intravenously in the attempted destruction of blood-flukes, and anyone undertaking to cure a case of bilharzia infection should be well acquainted with intravenous work as well as with the microscopic study of degenerating ova of schistosomes.

I have not experienced more than slight retching and salivation from injecting up to 2·25 c.cm. of anthiomaline to a child but, to avoid even this possibility, anthiomaline may be injected intramuscularly.

Eosinophil counts are of uncertain value in determining when the stouter male parasites are dead, and it is well to continue treatment for several days after all ova have disappeared from the centrifugalized deposit of an ample supply of urine. But experience would seem to show that in this combination a permanent cure may be obtained by injecting less than half a gramme of antimony metal.

The solution is clear and this gives it an advantage for intravenous use. Allied derivatives yield dark solutions, which render it difficult to decide when the point of the needle is inside the lumen of a vein.

The introduction of reliable antimony compounds, which are less irritating than tartar emetic in solution and equally potent, suggests a possible solution to the problem of curing schistosomiasis in sheep as well as elephantiasis in man.

I am indebted to Messrs May & Baker, Dagenham, for supplying me with a sufficient quantity of anthiomaline to investigate its use in schistosomiasis in South Africa.

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THE TREATMENT OF TUBERCULOSIS:

A Year's Progress.

A REVIEW of the entire literature on tuberculosis of the past twelve months would occupy an amount of space much beyond our own resources or our readers' desires, this survey will therefore follow the lines adopted in previous years and will deal mainly with medical treatment and diagnosis, with such points of general interest as may be germane to these aspects of the subject

A study of the three main types—human, bovine, and avian—of the tubercle bacillus (*Mycobacterium tuberculosis*) is presented by BIRKHAUG of the Pasteur Institute, Paris In each of nine strains investigated he found three different varieties of colony—rough, smooth, and chromogenic These varieties are interconvertible and their characters vary, but the smooth and chromogenic varieties differ in several respects from the rough variety, such as *p*H curves, agglutination, resistance to heat, etc In pathogenicity the chromogenic variety is avirulent for laboratory animals, while the other varieties vary in virulence for different animals Of the Calmette-Guérin bacillus (BCG) the rough variety is relatively avirulent except in very large doses, while the smooth variety is initially virulent but rapidly loses its virulence on culture and eventually becomes apparently permanently avirulent

Bovine Type—GRIFFITH (Med Res Council) and MUNRO (Glenlomond) give the histories of two families in each of which occurred two cases of pulmonary tuberculosis and in one a case of glandular tuberculosis in a child All five cases were infected with bacillus of the bovine type In one family the evidence was in favour of milk as the source of infection, the channel of entry being the alimentary tract In the second family the facts are more complex but the evidence strongly suggests familial infection In the case of the child the evidence is against transmission of infection from one of the parents

GRIFFITH and SMITH (Aberdeen) determined the types of bacilli in the sputum of 103 cases of phthisis pulmonalis from the rural and small urban districts of north east Scotland, including the Orkney and Shetland Isles The bacilli were of the human type in ninety cases and of the bovine type in thirteen All the strains from the bovine cases were typically dysgonic and highly virulent for rabbits Of the thirteen bovine cases seven were from the county of Aberdeen, four from Banff, and two from Moray The cases from the other counties yielded human type bacilli only

BLACKLOCK reports an investigation of 372 subjects with tuberculous lesions found in a consecutive series of 2500 children coming to autopsy in the Royal Hospital for Sick Children, Glasgow The

percentage incidence of tuberculous lesions was greater in children over three years, and girls were slightly more affected than boys In 239 cases the primary site of infection was in the thoracic tissues and this type of lesion was more frequent in subjects over three years Nearly all the children under three years of age who had primary thoracic lesions died of generalization of the disease Of 154 cases in which the organisms were typed, 148 were infected with human and six with bovine strains Of seventy-three strains isolated from primary abdominal lesions, thirteen were human and sixty bovine strains Of the total 236 strains isolated 167 were human and sixty-nine bovine strains, the highest percentage of bovine strains being found in the second year of life

Syphilis and Tuberculosis—GUILD and NELSON (New York) report an investigation of a large number of tuberculous patients which showed that the incidence of syphilis was 4 1 per cent in white patients and 21 per cent in coloured Without routine testing for syphilis its presence along with tuberculosis is easily overlooked Syphilis does not appear to predispose to tuberculosis PADGET and MOORE show that untreated syphilis prejudices recovery from pulmonary tuberculosis On the other hand it is reported that intensive antisyphilitic treatment was followed in a number of cases by the development of a previously unrecognized pulmonary tuberculosis with fatal results

Prognosis.—TRUDEAU (Saranac Lake, N Y) shows from a study of a number of cases that prognosis is greatly influenced by the extent of lung involvement In the exudative type of disease prognosis is more unfavourable than in the proliferative type The presence of cavities nearly doubles the probability of death within five years, while cavity cases showing improvement have a much more favourable prognosis Patients whose x-ray examinations are constantly favourable under sanatorium treatment have a good chance of being well within five years, but when fever is present in such cases the outlook is very unfavourable All this points to the importance of x ray examination from the point of view of prognosis

MYERS (Frimley) also stresses the importance of x-ray films as the most reliable guide to the spread or retrogression of actual tuberculous lesions, but he adds that the temperature chart, especially when considered in conjunction with these films, gives essential and valuable information Various types of lesion in chronic pulmonary tuberculosis give rise to characteristic changes in the temperature, but spread of the disease may occur in the absence of pyrexia Many quiescent cases suffer from frequent bouts of pyrexia without evidence of spread of the disease, and it is possible that pyrexia is often caused by infection of the lesions by organisms of the respiratory tract Study of x-ray films must therefore be made in conjunction with other clinical data

Diagnosis.—Histological diagnosis is discussed by CAPPELL (Dundee), who points out that when animal inoculation is not available there is danger in diagnosing tuberculosis merely from microscopical examination of tissues. Other factors must be considered, such as the age of the patient, the site of the lesion, and the evidence of other diseases, especially syphilis. Syphilitic lesions whose nature has been confirmed by W.R. and by response to treatment may be almost indistinguishable from tuberculous granuloma. In the breast, focal lesions accompanied by stasis of secretions may lead to areas of induration which microscopically closely resemble tuberculous changes.

Tuberculin Tests.—Since Koch introduced his subcutaneous tuberculin test in 1890, a number of modifications have been introduced, the comparative value of which has led to much discussion. Koch's test consists in the subcutaneous injection of increasing amounts of old tuberculin at intervals of a few days, beginning with a very minute dose and observing the smallest amount capable of producing a reaction. Other tests since introduced are: *Local Subcutaneous Test* (Stichreaktion), in which a diluted tuberculin is injected into the superficial cutaneous tissue, redness and infiltration constituting a positive reaction. *Conjunctival* or *Ophthalmo Reaction* (Wolff-Eisner ; Calmette), in which a solution of tuberculin is instilled into one eye. *Percutaneous Test* (Moro's ointment reaction), in which an ointment of tuberculin is rubbed into the skin. *Cutaneous Test* (von Pirquet): scarification of the skin and introduction of tuberculin. *Intracutaneous Test* (Mantoux), in which a drop of diluted tuberculin is injected into the skin.

CARSWELL (London) refers to certain criticisms of Koch's subcutaneous test made some years ago, in which it was argued that a negative reaction did not definitely exclude tuberculosis. He maintains that these criticisms were not well founded, and that sufficient detail had not been presented to warrant their acceptance. Koch's test, he holds, will do what was originally claimed for it, that is, a negative reaction will show that the case is not one of fresh or progressive tuberculosis demanding specific treatment. There is every reason to have confidence in its reliability, when properly performed, as a sound basis for the elimination of tuberculosis in cattle or in man.

KAYNE (London), whose previous work on this subject was referred to last year (*PRESCRIBER*, 1935, July, 228), discusses the value of the Mantoux test in relation to home-contacts. Children under two years with a positive Mantoux reaction should have their chests x-rayed ; if no lesion is seen they should be submitted to further investigation and observation. Mantoux-positive children from 2 to 5 years should also have their chests x-rayed. When no lesion is seen, subsequent action depends on whether the contagious person is at home or not. Mantoux-positive children over 5 years should have their chests x-rayed and should be kept under observation for

at least six months after contact has ceased Children whose Mantoux reaction is negative are dealt with according to the presence or otherwise of contagion in the home, if present the child should be separated and the test repeated every week for six weeks If contact has ceased, the test should be repeated as above but the child may remain at home

WESTWATER (Kelso) reports certain conditions that affect the intracutaneous test Measles and scarlet fever cause a temporary depression of sensitivity to the test this appears to be due to the action of the rash on the skin itself Such action is not shown by chicken pox, diphtheria, or whooping cough

Drawbacks hitherto attendant on the use of tuberculin for diagnostic purposes have been a variation in the composition of tuberculin and the presence of foreign protein which often masks the reaction These may be obviated by the use of the purified protein derivative isolated by Seibert (see PRESCRIBER, 1935, July, 229) This purified protein derivative is obtainable commercially as *Tuberculin P.P.D* in tablets of two strengths—0 0002 mg and 0 05 mg (Parke, Davis & Co) One tablet dissolved in one c cm of a special buffered diluent provides material for testing ten patients The 'first strength' or weaker tablet is used first, 0 1 c cm being injected intracutaneously on the forearm If no reaction occurs in the first test, a second is made with a 'second strength' tablet, 0 1 c cm of the solution being 250 times the 'first strength' dose If no reaction follows the second injection the reaction is negative

Tuberculin and Vaccines—Tuberculin is official in the British Pharmacopoeia 1932 as *Tuberculinum Pristinum*, Old Tuberculin, and is described as the concentrated filtrate from a fluid medium on which *Bacillus tuberculosis* has been grown The doses by subcutaneous injection are diagnostic, 0 001 to 0 005 ml , therapeutic, 0 000001 ml , gradually increased The human type is designated by the suffix T, and the bovine type by the suffix P T

The United States Pharmacopoeia of 1936 also contains *Tuberculinum Pristinum*, Old Tuberculin Tuberculin Koch, concentrated or crude tuberculin, which is described as a sterile solution in a special liquid culture medium of the soluble products of growth of the tubercle bacillus (*Mycobacterium tuberculosis*), containing about 50 per cent of glycerin Its dose, by intracutaneous injection, is 0 001 c cm

The Therapeutic Substances Regulations restrict the term 'tuberculin' to filtrates of cultures, the concentrated filtrate being known as 'old tuberculin' and the unconcentrated filtrate as 'tuberculin bouillon filtrate' Preparations made from the bacillary substance obtained by growth on artificial media, and consisting of suspensions of the killed organisms, are termed 'tubercle vaccines'

The British Pharmaceutical Codex contains such a preparation under the name of *Vaccinum Tuberculinum*, or Tubercle Vaccine,

which complies with these regulations. It is used in the treatment of tuberculous glands, tuberculosis of the bones and joints, tuberculous cystitis, and lupus Treatment should be commenced with the subcutaneous injection of the equivalent of $\frac{1}{1000000}$ to $\frac{1}{100000}$ mg of the dried substance, cautiously increased at intervals of 5-7 days It is not suitable for diagnostic purposes

Under the name of *Tuberculinum Novum*, the Codex groups a number of preparations made by methods designed to release the endocellular material of the bacilli It is added that there is *little evidence that they have any therapeutic or prophylactic* value

BURNELL-JONES (Royal Northern Hosp) discusses the use of tuberculin in the treatment of cutaneous tuberculosis He has used three tuberculins—T.A F , B E , and T R (Bayer), and he reports three cases, one of lupus vulgaris of the face and two of lupus verrucosus of the hands Whether tuberculin will cure lupus he cannot say definitely, but all three cases showed improvement and arrest of the disease and he thinks the work should be continued In one case improvement was not observed until after seven months' treatment All his cases were of long duration before tuberculin was started One case continued to improve with small doses the patient's tolerance should be the guide to increase of dose, and patients differ greatly in tolerance One patient showed a rise of temperature with as little as 0 0000005 c cm of tuberculin

Tubercle Vaccine BCG —The strain of bacillus known as *Bacille Calmette-Guérin* was isolated in 1924 by Calmette, of Paris, who cultivated it on a certain medium until it appeared to have lost its original virulence This culture of live avirulent organisms, known as ' BCG,' has been widely used on the Continent for the immunization of infants against infection, apparently with some success and evidently with little harm until the tragedy at Lubeck some years ago Since then the vaccine has been the subject of much investigation It is reported that a committee of bacteriologists and clinicians, under the chairmanship of Professor Marfan, has been appointed by the Pasteur Institute of Paris to study its value as a protective against tuberculosis in infants

Experiments with BCG vaccine are reported by CLAWSON (Minneapolis), who studied the effect on animals of both living and heat-killed organisms No toxic results were observed, either immediate or delayed In allergic animals large intravenous doses were followed by collapse and death, but ordinary doses had no toxic effect, nor had subcutaneous injections of the vaccine Clawson thinks that vaccination of human beings should be limited to those not having a positive reaction to cutaneous tests All methods seem to be safe except intravenous injection of living organisms

ARONSON and DANNENBERG (Philadelphia), in order to get an accurate estimate of its value, undertook a study of new-born infants in families with cases of manifest tuberculosis BCG was given

orally to these, while other infants, too old for oral vaccination, were treated as controls Of forty one vaccinated children only one died of tuberculosis, while of eighty-four unvaccinated children ten died from the disease No deaths from tuberculosis occurred in the children studied who were not associated with persons known to have manifest tuberculosis, and it is concluded that the administration of BCG to new-born exposed children may prove of value in reducing the mortality from this disease

RIST (Paris) is of opinion that the harmlessness of BCG vaccination is now unquestioned the real question is whether it affords protection against virulent infection Oral administration does not regularly immunize all the children and appears to be an uncertain method He cites Wallgren (see PRESCRIBER, 1935, July, 233), who gives the vaccine intracutaneously, and he concludes that this really protects uninfected children against virulent infection The immunity conferred is neither absolute nor lasting, and it is important that the children should be exposed to virulent infection when the vaccinal immunity is at its height The virulent bacilli are then absorbed and disposed of in the protected organism without causing any damage, and the result of those repeated virulent reinfections, provided they are not too massive, is to transform the relative and short lived artificial immunity produced by vaccination into a stronger and more lasting natural immunity

Nordalin —Though not strictly a vaccine, this preparation may suitably be mentioned here Nordalin is the outcome of work by Emil Scheitlin, of Basle, who showed that addition of sulphoguaiacolic acid to Koch's tuberculin in the presence of an anti-tuberculous serum produced a precipitate of a complex nature When this substance was allowed to act on the tubercle bacillus it penetrated the waxy sheath and acted on the cell elements, producing certain morphological modifications and a loss of virulence in the bacillus This sulphoguaiacolic precipitate has been placed on the market under the name of *Nordalin* which is issued in two forms Nordalin A is described as a sulphoguaiacolic acid precipitate of the plasma of immunized animals, with a minute quantity of Koch's tuberculin, in tablets for oral administration in prophylaxis and treatment Nordalin B is the same without tuberculin and is used in treatment only

TIPPETT (late of Nordrach upon Mendip Sanatorium), whose previous reports were mentioned last year (PRESCRIBER, 1935, June, 234), now records further cases The nordalin treatment, he says, does not claim to be a cure for every case of tuberculosis, because once the bacillus has invaded the human body and breakdown of the tissues has occurred the patient's vitality is greatly reduced The treatment, however, is so simple as to be worthy of an extensive trial Certain cases respond wonderfully well and it seems to help in making a positive sputum become negative and causing cavities gradually to close The patient usually puts on weight and is able to take

exercise without discomfort or rise of temperature. Some cases progress much more quickly than others, and where a case that was doing well seems to have become stationary he gives the patient a rest by suspending all specific treatment for a few weeks. If given to a case in which the disease has become arrested, nordalin treatment will prevent further relapses, and it is strongly recommended as a method of protecting adults and children who are in close contact with cases of consumption from the risk of infection.

Gold Therapy.—Since its introduction by Mollgaard in 1924, the double thiosulphate of gold and sodium, usually known as *Sanocrysin*, has been in general use for the treatment of pulmonary tuberculosis. Results on the whole have been favourable, and the opinion appears to be that its effect is beneficial so long as it is given in small progressive doses and its effects are carefully watched. Sanocrysin is a white crystalline salt, very soluble in water, and stable if kept cool, dry, and away from light. A yellow colour indicates decomposition and such crystals should not be used. The dose is progressive, commencing with 0·01 gm. and rising by degrees to 1·0 gm.; until a total of 15 mg./kg. has been reached. It is given intravenously, the required dose being dissolved in from 5 to 20 c.cm. of double-distilled water, and the strength of the solution ought never to exceed 5 per cent. Ampoules containing the required individual doses are available. Another salt of gold used for the same purpose is *Myocrisin*, or gold sodium thiomalate, which is given by intramuscular injection. Several organic salts of gold are also available.

Recent experience shows that gold salts are more lasting in their effects when administered in oily suspension than when given in aqueous solution. The oil suspension is eliminated slowly, allowing of continued improvement, but longer intervals are necessary between the courses, otherwise the patient may show symptoms of sensitization. A suspension in oil has been introduced under the name of *Oleo-Sanocrysin*. This is given intramuscularly, and is available in ampoules representing various doses from 0·02 gm. to 0·5 gm. *Oleochrysine*, or calcium auro-thioglyceryl sulphonate, contains 35 per cent. of gold and 4·53 per cent. of calcium in oily suspension. Both these preparations are given in small gradually increased doses.

KAYNE (London), as the result of visits to different centres on the Continent, reviews the results of the use of sanocrysin. Regarding severe constitutional symptoms as a relative contraindication, he concludes that the clear indications for gold therapy are as follows: (1) Recent lesions of the exudative type; when cavitation is present sanocrysin may be used, but an artificial pneumothorax should be induced without delay. (2) Recent exudative lesions in association with old-standing disease. (3) In patients in whom suggestive shadows are found during routine examination in the absence of definite clinical evidence of activity, observation may be combined with judicious ambulatory gold therapy. Large initial doses are too

dangerous, a start should be made with 0 05 gm, gradually increasing by 0 05 gm and then by 0 1 gm until a dose of 0 5 gm has been reached If no obvious improvement is observed after four or six weeks, or a total of about 4 0 gm, continuance is not justified

PETERS and SHORT (Bristol) present a statistical study of the results of gold treatment in a group aged 16 to 26 during five years Their figures are rather disappointing The differences in results between the period covered, and a similar age-group during the five years prior to the use of gold, are negligible Many cases seemed to do extremely well, but so did many before the introduction of gold therapy While admitting the difficulty in assessing the value of any form of treatment for pulmonary tuberculosis, as results differ in every case, they are forced to the conclusion that chrysotherapy is of no appreciable value

Actinotherapy.—While much diversity of opinion exists, the majority of workers are agreed that good results follow light treatment when applied to selected cases of pulmonary tuberculosis This conclusion is arrived at by FURNISS (London), who reviews the subject generally When a patient is weak with much toxaemia and hectic fever, the sun bath is likely to do more harm than good Miliary tuberculosis is a definite contraindication Surgical tuberculosis, on the other hand, responds very well to light treatment

COULTER and CARTER (Chicago) undertook a study to determine the value of sunlight and artificial radiation in the treatment of pulmonary tuberculosis The clinical results of this study showed, in their opinion, that no definite benefits are to be derived from the use of ultraviolet radiation in the treatment of active cases or in cases following thoracoplasty In cases of thoracoplasty with delayed wound healing, local ultraviolet irradiation with a carbon arc lamp increased the growth of healthy granulation tissue and the tendency to epithelization So long as the dosage is carefully regulated, the treatment appears to be without danger Sun treatment (heliotherapy) is not practicable near a large city on account of the atmospheric conditions

A very full review of the subject is contributed by MAYER (New York), who concludes that pulmonary tuberculosis *per se* is not an indication for light therapy, though stationary pleural tuberculosis has often been helped by it In tuberculosis of the bones, intestine, larynx, etc, benefit is undoubtedly obtained, but this is not due to ultraviolet rays alone, as the visible and infra red rays play a part In tuberculosis of the skin, lupus vulgaris alone responds Lupus erythematosus does not respond and may be aggravated Of the other forms of tuberculosis some are known to be resistant to light therapy, while others deserve a trial of such treatment

MILLAR (Melbourne) speaks highly of the use of ultraviolet radiation in the treatment of tuberculous laryngitis Commencing with irradiation for half a minute, the dosage is gradually increased to five minutes The tolerance of the pharynx increases with each

treatment The hypertrophic type responds best, next comes the ulcerative type, and lastly the oedematous lesions

TROUP (London) recommends irradiation treatment for tuberculosis of the nasal sinuses The forms he employs are (1) infra-red rays applied locally, (2) ultraviolet rays applied post nasally and intranasally, (3) ultraviolet rays applied to the whole body Success depends on accurate dosage, since varying stimuli evoke varying responses in different cases

Dietetic Treatment.—The salt-free regimen introduced by Gerson, especially as modified by Sauerbruch and Herrmannsdorfer, is still attracting attention, though to a less degree than hitherto In addition to being salt free, the diet is almost entirely vegetarian, its aims being (1) limitation of mineral salts, (2) reduction of carbohydrates, and (3) administration of vitamins

The original Gerson diet, which was much more rigorous than the modification mentioned above, is the subject of a monograph by GERSON himself, in which he sets out details of the regime and describes in detail over fifty cases treated at the hospital in Berlin and later by himself in Austria He believes that his diet will induce healing of pulmonary tuberculosis even in advanced cases provided that sufficient functioning lung tissue remains, that the patient's general condition is not too bad for him to take the diet, and that complications such as lardaceous disease are not present He insists that success depends on scrupulous observance of details, which are fully set out in the book Unfortunately he found great difficulty in keeping his patients on the prescribed regime in many cases they refused to continue the diet and even physicians seem to have turned a blind eye to its non observance

Surgical Treatment.—O'SHAUGHNESSY and CRAWFORD (Preston Hall) discuss the induction of temporary paralysis of the diaphragm by phrenicothlasty, or crushing of the phrenic nerve, and describe a case in which it was performed with good results They say that in 43 out of 44 cases in which the method was employed it produced a paralysis persisting for an average period of six months, and it appears to give more consistent results than the alternative measures of phrenic evulsion and phrenicotomy

PURCE and CLARKE (Belfast) present an analysis of their results in 316 cases in which phrenic evulsion was performed, either alone or as an adjunct to artificial pneumothorax When performed alone, improvement usually resulted and healing of cavities took place in 33 per cent of cases Multiple cavities seldom healed, nor did cavities more than two inches in diameter, 50 per cent of early type cavities healed but only 4 per cent of the late type The operation appears to be of most service when the lower half of the lung is diseased When used as an adjunct to artificial pneumothorax a satisfactory collapse of the lung was frequently obtained

Thoracoplasty is dealt with by YOUNG (London) This method,

he says, should be considered in all cases of pulmonary tuberculosis that have not achieved arrest of the disease by other means, but certain conditions must be fulfilled before it can be recommended The lesion must be of the type that will heal if mechanical impediments are removed; if lesions are present in the other lung they must be inactive; fresh 'flares' in apparently healthy areas must be improbable, the patient must be fit for the operation and have reached the most favourable moment for its performance, technical conditions must be satisfactory, and it must be clear that a good functional result will be obtained The mortality from the operation, though small, is not negligible Thoracoplasty represents the last stage in the active treatment of any tuberculous lesion in the lung An error made in selection of the case, or the stage in which it is to be performed, cannot be repaired, but in no form of treatment will skilled collaboration between physician and surgeon be more amply repaid

Miscellaneous Methods.—GAUVAIN (Alton) calls attention to the value of sea bathing in the treatment of properly selected cases of surgical tuberculosis To get the best results short immersion in cold sea water is better than long immersion in warm sea water Metabolic activity is increased, repair is hastened, muscular tone is improved, recalcification of lesions is stimulated, tuberculous glands are more rapidly absorbed, and in sinuses there is increase of discharge followed by rapid healing The evolution of tuberculous abscesses is often checked and healing is hastened

Merthiolate.—LAMBERT (Saharanpur, India) reports on the use of 'merthiolate,' or sodium ethoxymercury thiosalicylate, which was fully described in our review on Antiseptics last month (PRESCRIBER, 1936, June, 215) He describes eight cases, including pulmonary and other forms of tuberculosis, treated with intravenous injections of merthiolate, 5 c cm being injected on alternate days All the cases, except one which was probably beyond human aid, showed reduction or stabilization of the temperature, while in one case a gain in weight and subjective improvement were recorded Whether this was due to the antiseptic properties of the drug or merely to the antipyretic action of its salicylic component, Lambert is unable to say, but he thinks the drug is worthy of further investigation

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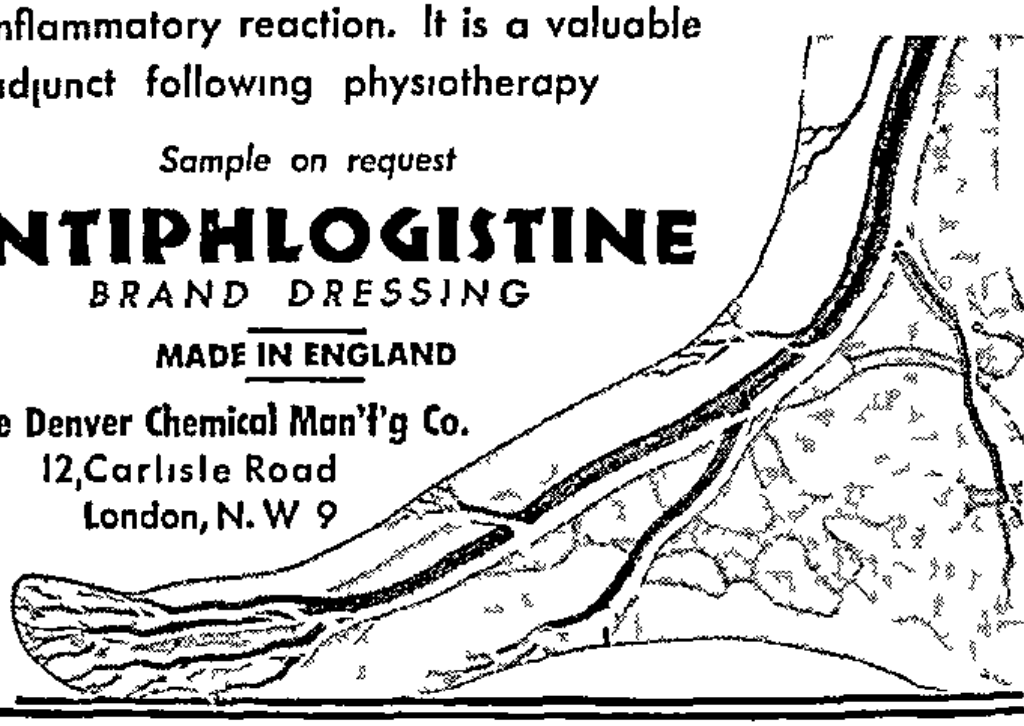
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Dysmenorrhoea: Insulin.—A. ALTSCHUL (New York) reports that in a group of 12 patients, all nulliparas, suffering from primary or essential dysmenorrhoea, 10 received practically total relief from menstrual pain by using insulin from 3 to 7 days before or during the period One patient was only partially relieved, while another obtained relief from one brand of insulin and not from another — *J.A.M.A*, Apr. 18, '36, p 1380

NEW REMEDIAL AGENTS.

Benzedrine in Narcolepsy.

ABOUT two years ago brief reference was made in these pages (PRESCRIBER, 1934, June, 223) to a synthetically prepared base known as *Benzedrine*, which was reported to have an action similar to that of ephedrine or adrenaline It bears a close chemical relationship to these substances, being desoxy-nor-ephedrine or β-phenylıso propylamine, C_6H_5 CH_2 CH NH_2 CH_3 It is a colourless mobile liquid, soluble in ether and alcohol and slightly soluble in water

Benzedrine was originally introduced as a substitute for ephedrine in the treatment of head colds, sinusitis, hay fever, etc A one per cent solution in liquid paraffin is used as a nasal spray or for instillation into the nasal passages SCARANO reports its use in 100 cases of rhinitis, including the acute, chronic catarrhal, chronic hypertrophic, and atrophic varieties The best results were obtained in cases with obvious congestion of the nasal mucosa and turbinates associated with profuse watery discharge The percentage of benefit was somewhat greater in the acute than in the chronic cases

Pharmacological studies of this compound have shown that it has a more stimulating effect than ephedrine on the higher nerve centres and that it has the property of antagonizing the action of barbitone and of producing insomnia in human beings This has led to its application in the treatment of narcolepsy, a condition marked by an uncontrollable desire for sleep, which occurs at intervals Its low toxicity and its prolonged action being in its favour, a study of its action in this condition was made by PRINZMETAL and BLOOMBERG (Boston, Mass) Nine patients with typical histories of narcolepsy were selected Complete relief from attacks of sleep and practically complete relief from cataplexy followed the administration of suitable doses Compared with ephedrine, benzedrine is about three times as effective Usually a moderate dose such as 30 mg ($\frac{1}{2}$ grain) afforded complete relief from symptoms, even in cases in which large single doses (80 to 150 mg) of ephedrine failed to give relief As individual response to benzedrine appears to vary, it is recommended that a small dose (10 mg or $\frac{1}{6}$ grain) be given at first, the amount being gradually increased until an optimum effect is obtained

The same workers are studying the effect of benzedrine in other neurological conditions, especially certain forms of asthenia, and their results will be published in due course

Attention has been called by PEOPLES and GUTTMANN (Maudsley Hosp) to the effect produced by benzedrine on the blood-pressure The drug appears to produce a fluctuating rise in blood pressure, which in turn has certain psychological effects in mental patients They are of opinion that while benzedrine is an effective and a promising therapeutic ally, further observations of its action are

necessary to determine the exact nature of its by-effects in such cases, and to see if it is suitable for permanent administration.

PEOPLES, S. A., and GUTTMANN, E. Hypertension produced with benzedrine: its psychological accompaniments. *Lancet*, 1936, May 16, 1107-1109.
PRINZMETAL, M., and BLOOMBERG, W. The use of benzedrine for the treatment of narcolepsy. *J.A.M.A.*, 1935, Dec. 21, 2051-2054.
SCARANO, J. O. Benzedrine in rhinitis. *Med. Record*, 1936, Feb 19, 161.

New Drugs and Preparations.

[Under this heading are given brief notices of new non-secret products as they appear on the market or are mentioned in medical literature. The notes are intended for reference only, and must not be taken to imply anything in the nature of a recommendation. In most cases the information is derived wholly or mainly from makers' advertisements.]

Embryonin.—A placental extract for use in the prevention and treatment of measles (Bioglan Labs., Hertford).

Esmodil.—Trimethyl-methoxypropenyl-ammonium bromide; a white crystalline powder soluble in water. It differs slightly from acetylcholine in its properties, yet resembles it in its stimulant action on the parasympathetic nerve-endings. Recommended in postoperative ileus and retention of urine. Ampoules containing 1 c.cm. of a 3 per mille isotonic solution (Bayer Products, London).

Fangat.—A therapeutic mud (fango) from the volcanic Eifel range in Germany. In three forms: pure, salicylic, and ichthyol (Coates & Cooper Ltd., London).

Fortamin.—A tonic containing vegetable bitter reinforced with calcium glycerophosphate. The bitter content is the result of research by Professor Wiechowski of Prague, and is designed to restore normal sensitivity towards physiological endocrine stimulus. Fortamin contains no strychnine, arsenic, or caffeine. Bottles of 175 c.cm. (Schering Ltd., London).

Immune Globulin (Human).—An extract of human placenta for use in the prevention and treatment of measles; described in THE PRESCRIBER, May 1936, p. 201 (Lederle Labs., New York; Agents, C. F. Thackray Ltd., Leeds).

Magsorbent.—Magnesium trisilicate; antacid and absorbent in treatment of peptic ulcer and acid dyspepsia (*B.M.J.*, Jan. 25, '36, p. 143; Feb. 1, '36, p. 205; Feb. 8, '36, p. 254). Dose, one to two teaspoonfuls of the powder or one to three tablets (Kaylene Ltd., London).

Mandelix.—An elixir of ammonium mandelate containing in 2 drachms the equivalent of 3 gm. (45 grains) of mandelic acid, for treatment of urinary infections (British Drug Houses Ltd., London).

Neoket.—A granular preparation containing mandelic acid, sodium bicarbonate, and sodium acid phosphate, with flavouring. For treatment of urinary infections. Dose, two teaspoonfuls, equivalent to 45 grains mandelic acid (Boots, Nottingham)

Raderma Ointment—Contains certain vegetable extracts in a basis of lanolin, soft paraffin, and ceresin, for protection of the skin against burns from radium, x rays, and ultraviolet radiation (H K Labs, London)

Recresal—A preparation of sodium phosphate in tablet form, recommended as a muscle and nerve tonic and to stimulate wound healing Dose 2 to 3 tablets twice daily (Coates & Cooper Ltd., London)

Skol—A liquid astringent antiseptic, containing according to the published formula extract of galls, menthol, phenol, glycerin salicylic acid, alcohol, and water Recommended for treatment of skin conditions such as eczema, burns, abrasions, cuts, etc., also as a mouthwash or gargle (Skol Products Ltd, London)

Spasmolyth.—Powders containing phenazone, phenacetin, caffeine, grindelia, and cereus grandiflorus, for oral administration in asthma (Curzon Pharmaceuticals Ltd, Worksop)

Stellidin—A 4 per cent aqueous solution of histidine monohydrochloride for injection in the treatment of peptic ulcer (May & Baker, Dagenham)

Stypven—Snake venom (*Vipera russelli*) for treatment of bleeding in haemophilics (see PRESCRIBER, Jan '36 p 15) In bottles of 1 and 5 c cm accompanied by ampoules of sterile distilled water with 0 5 p c. phenol to make a suitable dilution for topical application only (Burroughs Wellcome & Co, London)

Super-D Oil (Crookes)—A natural liver oil of high potency, from the livers of fishes of the N O Scombridae containing 50 000 international units of vitamin D and 48 000 units of vitamin A per gramme In capsules containing 3 minims, also in vials of 5 c cm (British Colloids Ltd, London)

Thevetin—The glycoside obtained from the seeds of *Thevetia neriifolia*, or yellow oleander, described in THE PRESCRIBER, Nov 1935, p 359 Action similar to digitalis but more rapidly developed Dose, 3 cat units (2 75 mg) thrice daily, intravenously, until signs of digitalization become evident, then 3 cat units every other day Ampoules, 2 c cm, containing 3 cat units (Eli Lilly & Co Ltd, London)

Tonergeticum—A nerve tonic containing phosphorus, quinine, kola nut, piscidia, viburnum, hops, with small quantities of copper, iron, and manganese salts, magnesium and bromine Dose, one teaspoonful (Homburg Pharma Ltd, London)

Transcutan—A concentrated solution of mineral salts obtained from the natural springs of Kreuznach, containing iodine, bromine, etc, with terpenes, for use in baths *Transcusalve* is an ointment containing the same ingredients with salicylates and camphor (Transcutan Ltd, Leeds)

Tridestrin—Tablets containing a form of oestrin found to be effective when given orally Indicated in all conditions in which oestrin is required and where injection is not feasible (Paines & Byrne Ltd, Greenford)

Tussipect.—An expectorant preparation of the root of *Primula elatior* (cowslip) Supplied as syrup (dose 1 to 2 teaspoonfuls) and drops (dose 10 to 15 drops) Said to be specially suitable for children for whom the dose is proportionately less (Beiersdorf Ltd, Welwyn Garden City)

REVIEWS OF BOOKS.

Symptoms and Signs in Clinical Medicine By E Noble Chamberlain, M D Pp 424 (Wright 25s)

It is perhaps right to say that of all the subjects in the medical curriculum Clinical Medicine is one of the most difficult for the student He has to master a long series of investigation methods and to apply his mind to the meaning to be deduced from them Appearances and sounds hitherto outwith his experience have to be appreciated, differentiated one from the other, and their varying values assessed, and all this is very difficult and takes time, patience, and concentration. Little wonder therefore that the student welcomes a guide to his ward work, especially when the guide leads him quickly along, beginning with the relatively easy and ending with the more abstruse Dr Chamberlain has written such an easily read book with a large amount of useful, indeed essential, clinical information, without undue detail and always with clear definition of language The illustrations, 282 in number, are well chosen and simplify the text J O

Poisons Law A Guide to the Provisions of the Pharmacy and Poisons Acts, 1852 to 1933, etc By Hugh N Linstead Pp 444 (Pharmaceutical Press 5s)

One sometimes wonders whether the present tendency to complicated legislation is good That a thorough revision of our Poisons Law was overdue every one will admit, but the law on poisons, as it came into effect on May 1 of this year, is surely carrying legislation to extremes What with its numerous schedules, rules, and forms, with its poisons that are or are not poisons, with its provisions for storing, labelling, recording, and inspecting, it is doubtful if any one handling these substances will be able in future to avoid breaking the law It will of course provide work for the lawyers and for the inspectors, and it has already given a good job to the writers of books

The present book is the work of the Secretary of the Pharmaceutical Society and is designed mainly for the guidance of pharmacists, who are most closely affected by the new legislation The opening chapters show how the law on poisons has developed in a more or less casual manner and explain why a complete revision of existing law was necessary The author then gives an exposition of the new poisons law, while many details are included in the Appendices Such a book is certainly necessary for those who have to interpret the new law

The Anti Drug Campaign An Experiment in International Control By S H Bailey Pp 264 (King & Son 12s)

This is a matter of-fact account of the measures officially adopted to control the trade in opium, coca, and cannabis, and their derivatives, the word 'drugs' being used in the restricted sense of 'dangerous drugs' Mr Bailey is Senior Lecturer in International Relations, London School of Economics He describes the evil and shows the necessity for control, then he relates the measures adopted by the Hague Convention and the Geneva Agreement, the difficulties encountered and the obstacles to effective control, the 'Offensive of 1931,' and the duties of national administrations The work of the League of Nations is explained The

history of the international campaign, he tells us, shows that from a tangle of mixed motives a constructive purpose has emerged and seems destined to prevail More than a third of the book consists of Appendices giving the various enactments, etc, verbatim For those who wish to study the subject intensively this book will be useful T S

Dictionary of Organic Compounds Edited by I M Heilbron, *D S O*, D Sc, F R S, etc, and H M Bunbury, M Sc, A I C Vol II Eccaine—Myrtillin Chloride Pp 846 (Eyre & Spottiswoode £6 6s per vol, £15 15s the set of three vols)

In our review of the first volume of this work on its appearance a little over a year ago we referred to its importance in view of the great developments in organic chemistry during the present century The second volume ably maintains the high standard of the first The authors have devoted additional attention to compounds of interest to biochemists while the compounds used in medicine are very numerous For example, one finds references to glutathione, histidine, hippuric acid, insulin (though this has only five lines), evipan, the alkaloids of ephedra and of ergot, and many others It is, however, in respect of the more out of the way compounds that this book is of real value, and after a year's experience of the first volume we can say that for such items we have never turned to it in vain The real value of such a work can only be assessed in this way The second volume contains about 120 pages more than the first It has no supplementary list, the authors having managed to include the necessary additional items while going through the press The third volume, which is expected to be published during the present year, will complete the work As a model of elaborate conciseness this work stands supreme T S

Physical Aspects of Organic Chemistry By William A Waters, M A, Ph D, with an Introduction by T Martin Lowry, D Sc, F R S Pp 501 (Routledge 25s)

During the past fifteen years or so great changes have taken place in our conceptions of physical chemistry, changes which have materially affected that most important section of the science, organic chemistry The fresh light thrown upon organic combinations has already been of service to medicine, and will continue to do so more and more as time goes on As a guide to the present position of organic chemistry in its new aspect this book is complete and informative It was started as a joint work by Dr Waters and Professor Lowry, but the second worker found it impossible to continue his share, and now contributes an introduction The conception of the electrical properties of the atom and the molecule and its effect on chemical reactions is well shown and the book will be most useful to biochemists and to those numerous medical men who now find a knowledge of chemical reactions to be essential to a true understanding of the workings of the human organism T S

Antoine Lavoisier The Father of Modern Chemistry By Douglas M Kie, Ph D, B Sc Pp 303 (Gollancz 10s 6d)

The outstanding facts of the life of Lavoisier are familiar to most of our readers and call for no repetition here Their importance, their variety, and their dramatic significance lose nothing in the re-telling Dr

M'Kie has written *con amore* and has produced a thoroughly readable and reliable work, readily understandable by any layman who cares for scientific reading. It earns well-merited approbation from Prof. Donnan, who contributes an introduction and who describes the author as taking 'a high place amongst the historians of science.' We would suggest that Dr M'Kie should now turn his attention to Roger Bacon, an equally great but unaccountably neglected pioneer of science about whom no comparable biography exists. As one reads one realizes anew how the discovery of oxygen and of the nature of combustion was the greatest chemical discovery of the 18th century and truly the foundation of chemistry as we know it. It is a pity Lavoisier dabbled in politics. His tragic end is dramatically described. R. C. O.

Disease and Destiny. By Ralph H. Major, M.D. Pp. 338. (Appleton. 12s. 6d.)

Although a popular work, this book has a considerable value for the medical man inasmuch as it not only provides light entertainment of a kind specially interesting to him but also affords much miscellaneous information of an unusual nature. We are reminded how bad were the 'good old days' when pestilence swept across continents and populations stood helpless in the grip of epidemics Such scourges as the Black Death, Jail Fever, and Leprosy are dealt with in their proper historic setting. A good illustration of the effect of disease on history is Henry VIII's syphilis, resulting in so many still-born children, in his divorce, in his quarrel with the Pope, and in political developments traceable to the present day. This is a lively, informative, and absorbing work, worth buying and keeping for reference. R. C. O.

MEDICAL RESEARCH COUNCIL SPECIAL REPORTS.

No. 207. *The Localisation of Sound.* By H. E. O. James, M.Sc. (H.M. Stationery Office. 9d.)

This is the third Report issued by the Committee upon the Physiology of Hearing. The conclusions reached are important, both theoretically and practically, especially at a time when accurate and rapid perception of sound is becoming daily more necessary.

No. 208. *The Course of the Oesophagus in Health, and in Disease of the Heart and Great Vessels.* By William Evans, M.D. (H.M. Stationery Office. 2s. 6d.)

This Report is designed with a view to its value in diagnosis. The contours of the gullet are noted in detail, its curves being explained in terms of surrounding structures. The distortion caused by gross aneurysms of the aorta is variable in form and in degree; in less advanced disease minor distortions of more fixed pattern occur which are of value in early diagnosis. Progressive morbid changes can thus be gauged in an accurate manner.

No. 209. *Experimental Epidemiology.* By M. Greenwood, M.D., A. Bradford Hill, D.Sc., W. W. C. Topley, M.D., and J. Wilson, M.B., Ch B. (H.M. Stationery Office. 3s. 6d.)

This Report is based on researches pursued during the past eighteen years under the auspices of the Medical Research Council. It is a study

of the behaviour of infected herds and their response to various external influences In this way the problems associated with epidemics have been investigated with a view to their application to human beings Many questions regarding resistance, prophylactic immunization infectivity and such like have been answered, and while the Report is mainly a preliminary survey of the field many points have been proved and others are discussed A 'summary and conclusions' occupying ten pages is given at the end of the Report

The University Tutorial Press has published a second edition of A First Course in Human Physiology, by G N Meachen M D (3s 6d) The book provides a sound general introduction to the study of physiology, presented in a manner suitable for schools continuation classes and for students contemplating the study of medicine The text matter is lucid and the illustrations are clear and mostly diagrammatic The author resists the temptation to go into detail the chapter on the Endocrine Glands for example occupies only five pages yet it contains all the information necessary for its supposed readers The book is admirably adapted to its purpose and has the advantage of being very reasonable in price

Family Medical Insurance is the title of a thoughtful essay by J Lachlan Cope (Bale, Sons & Danielsson 2s) The author's main points are the family, not the individual as the centre of the scheme for treatment, the necessity for skill in diagnosis the availability to all of consultants and institutional services—medical surgical and obstetric—whenever necessary Present day physicians he thinks, are not sufficiently skilled in diagnosis and this must be corrected by remodelling the curriculum While the author's ideas are perhaps Utopian his sincerity cannot be doubted and his advocacy of post-graduate hospital residence will be warmly approved Ways and means and finance are of course mentioned but their treatment is not sufficient to show clearly how the cost is to be met Still the author's object is to awaken interest in his ideas and perusal of his pages is well worth while

Dr Morath A Novel by Max Rene Hesse, has been rendered in English by Edward Crankshaw (Allen & Unwin 8s 6d) We are told that over 29 000 copies have been sold in Germany The scene is laid in South America where Dr Morath a German hospital surgeon is seen as an idealistic young man endeavouring to uphold his professional honour in the teeth of a money loving environment Wealthy patients are jockeyed into unnecessary operations for the sake of fat fees an old theme this and now stone cold The heroine like the hero is well drawn and full of vitality and in spite of her vulgarisms she is at last wedded to the doctor Perhaps the book's chief interest is in the vivid pictures of life in South America

The Report for 1935 of the Institute of Medical Psychology (The Tavistock Clinic) is now to hand and provides interesting reading We learn of the success which has been met in dealing with one of the greatest of social problems the early manifestations of psychic disorder The successful efforts of Kraepelin in Munich did much to prevent mental disorders from becoming stabilized and efforts of this kind are to be welcomed and merit public control and support

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The Prescriber.

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DRUGS: ANCIENT AND MODERN.

DURING the past few weeks two public addresses of widely different purport, yet both having a bearing upon therapeutics, have been recorded. Madame Joliot-Curie, daughter of the discoverers of radium, has announced the synthesis of radioactive elements and its possible therapeutic application, while Mr Harold Deane, Chairman of the British Pharmaceutical Conference, has presented a modern outlook to the old question of the cultivation of vegetable drugs. Both these addresses have a bearing on therapeutics which in these days cannot be disregarded.

It is over thirty years since the Curies announced their discovery of radioactivity, a discovery that almost completely revolutionized our conceptions of physical chemistry and at the same time added a new weapon to our therapeutic armoury. Their daughter now shows how it is possible to transform aluminium into phosphorus by bombardment with alpha rays. The phosphorus so produced, however, has a lower atomic weight than ordinary phosphorus—30 as against 31—and its atoms are very unstable. As phosphorus is closely associated with the more highly organized cells of the human body, this new radioactive phosphorus may have a special therapeutic value. So far the quantities obtained have been very minute, but the practical application of the discovery appears to be only a question of time, while the extension of the principle of synthetic radioactivity to other elements offers a field for research having immense possibilities.

Mr Deane's address dealt with a different aspect of therapeutics, but one that is equally important from the

point of view of future research. Increase in the use of synthetic remedies and active principles has led to a decline in the employment of vegetable drugs. It is fairly certain, however, that such products as opium, digitalis, and belladonna will survive, while others, like the age-old ergot and the equally ancient ephedra, are experiencing a revival of interest. If this interest is to be maintained and the therapeutic properties of these plants are to be fully developed, the question of their cultivation should receive greater attention. At present medicinal plants are grown rather than cultivated: the same attention is not paid to their development as is given to fruit-trees or cereal crops. This matter requires much investigation, for it is relatively easy to brighten the colour of a flower or to improve its scent, but no one knows exactly how to improve its medicinal value. Research might well be directed along such lines.

It may be that these two subjects are more closely linked than would appear at first sight. The subject of radioactivity is in its infancy while vegetable cultivation is one of the most ancient of the arts. But the sciences are daily becoming more interdependent, and it is possible that suitable application of the principles of the one may lead to a new conception of the other. If the new synthetic radioactivity is to have application to the cells of the human organism, may it not be found to assist the growth and development of plants? This of course is mere speculation, but it is not beyond the bounds of possibility.

Benzedrine.—In the article appearing in our July issue, page 246, the impression is given that benzedrine is issued in liquid form. This is not strictly correct: the form in which the drug is supplied for internal use is the sulphate—β-phenylisopropylamine sulphate (isomyn sulphate). This is issued in the form of tablets under the name of '*Benzedrine*' *Brand Tablets*, each of which contains 10 mg. ($\frac{1}{6}$ grain). Given orally in doses of one to three tablets, this drug has a stimulating effect on the central nervous system; it relaxes smooth muscle of the gastro-intestinal tract and in the higher dose range produces a sustained rise in blood-pressure. The tablets have been used with success in narcolepsy, and investigations are in progress with a view to further evaluation of their usefulness. The distributors in this country are Messrs Menley & James Ltd., London.

RECENT WORK ON SYPHILIS.

An Abstract Review.

RESEARCH on the causal organism of syphilis is still in progress. The organism was discovered in 1905 by Schaudinn and Hoffmann, who named it *Spirochaeta pallida*. A more accurate classification of the spiral protozoa caused its name to be changed to *Treponema pallidum*, and later to *Spironema pallidum*, one or other of these two names being now generally used. The term 'spirochaete' is still retained as descriptive of the whole class of spiral organisms. In 1912 McDonagh suggested that this organism is not in itself the cause of syphilis, but that it is merely a phase of a protozoon which he named *Leucocytozoon syphilidis* (see PRESCRIBER, 1916, Mar., 55). More recently Levaditi and associates (Pasteur Inst., Paris) expressed the opinion that the organism exists first in an invisible form (*phase aspirochétienne*), when the tissues are inflamed but show no spirochaetes, and that later a second stage supervenes (*phase tréponémique*) in which the spirochaetes appear and multiply rapidly. The invisible form transmits the disease only in cases in which the spirochaetal form is not found. Lépine, a pupil of Levaditi, has since shown that *T. pallidum* on culture rapidly loses its virulence and fails to transmit the disease to animals, although it renders the Wassermann reaction positive. Further, in general paralysis the cerebral cortex is rich in spirochaetes, yet inoculation with the brain tissue of paralytics has never succeeded in transmitting syphilis. Lépine holds, therefore, that the invisible form and not the spiral form is the agent responsible for transmission of the disease in all cases. Levaditi does not support this view, maintaining that in culture spirochaetes change their character and that the brain tissue of paralytics may contain spirochaetes so modified as to be incapable of transmission. The subject is fully reviewed by SIMON, who is inclined to support the views of Levaditi.

The effect of syphilis on pregnancy is discussed by MCCORD (Atlanta, Ga.). A clinical study of 2150 cases leads him to the conclusion that pregnancy does not affect the reliability of the Wassermann reaction, which should be a routine procedure. Suitable treatment will ensure delivery of a child free from syphilis in 95 per cent. of cases; treatment should be mild but continuous. A strongly positive cord W.R. done on the child is indicative of congenital syphilis; a negative cord reaction is of little value.

In a similar study COLE and associates (Washington, D.C.) show that congenital syphilis is practically a preventable disease, its prevention being dependent on the routine, early, and repeated use of the serological test on every pregnant woman and on adequate early treatment once syphilis has been diagnosed. The pregnant syphilitic woman tolerates antisyphilitic treatment well. When

treatment is begun before the fifth month the chances in favour of the child are much greater

Dealing with antenatal treatment, SYMINGTON (Leicester) describes fifty cases and regards the outlook as hopeful Of these patients 44 had live full-time births, and of 53 babies whose blood was tested 51 gave negative reactions ELLIOTT (Colchester) reports a case in which syphilis was transmitted to the third generation

The treatment of congenital syphilis is discussed by SMITH (Johns Hopkins Univ), who regards early cases as curable It is important to start treatment at an early age a child whose treatment is started under 6 months and who receives fifty injections before the age of 2 years has an 84 per cent chance of complete recovery

Discussing prognosis, NABARRO (London) says that if treatment is started within six months of birth a complete recovery may usually be expected Routine blood testing during pregnancy and antenatal treatment when necessary would render congenital syphilis non-existent in a generation Congenital neurosyphilis offers an almost hopeless prognosis It is interesting to note, however, that TENNENT (Maudsley Hosp) recently reported that of twenty-seven such cases under his care, five had shown considerable improvement under treatment with malaria and tryparsamide (see Neurosyphilis)

INGRAHAM (Philadelphia) deals with the diagnosis of infantile congenital syphilis during the period of doubt Treatment offers the best hope of recovery if instituted during the first two months of the child's life, but the difficulty of diagnosis during these two months is very great The earliest and commonest sign is nasal obstruction during the first few days Splenomegaly is a sign of value, but skin lesions and osteochondritis are never present at birth Malnutrition is suspicious, as also is elevation of temperature The Wassermann test has no clear-cut value during the first few weeks it may be positive in a healthy child and negative in syphilitic cases The blood sedimentation rate is suggestive only, and dark-field examination reveals spirochaetes in 20 per cent of infants born of syphilitic mothers In cases where congenital syphilis is possible, Ingraham advises a judicious use of these various signs during the first week of life if this is done the diagnosis will be sure in 75 per cent of cases before the end of the second month

The question of the transmission of syphilis by blood transfusion is discussed by several workers MORGAN states that the disease is transmissible in this way only when the virus is present in the donor's blood Spirochaetaemia is known to occur only during the early stages of the infection before the development of latency, or during pregnancy in the chronic disease Present knowledge does not permit a diagnosis of transfusion syphilis in the absence of these stages of infection in the donor MANDELBAUM and SAPERSTEIN (Bellerose, N Y) report a case of acute gummatous osteomyelitis in which syphilis was acquired through the medium of a blood transfusion The donor was not in the active phase of syphilis at the time of the transfusion, nor has he subsequently shown active lesions

Diagnostic Reactions —In an exhaustive review of the subject of serum reactions, OSMOND (St Thomas's Hosp) makes some points that are worth recording The value of any test depends on two factors—the skill and experience of the tester and the specificity and sensitivity of the test Few tests are more capable of error than the Wassermann, yet this test is often done in a most perfunctory manner A laboratory should perform at least fifty tests a week if the results are to be reliable Barring yaws and relapsing fever, and sometimes leprosy, the complement-fixation test is practically specific for syphilis under acceptable technical conditions Only three results are possible—positive, negative, and doubtful—the term 'weak positive' should not be used In primary syphilis a positive reaction may be expected on the seventh day In secondary syphilis the percentage of positive reactions is practically 100 The greatest value of the test is in the detection of latent syphilis In tertiary syphilis the percentage of positive reactions varies with the organ or part involved In neurosyphilis a high percentage of positives may be expected, but it should be remembered that a negative reaction may be associated with a positive spinal fluid or vice versa As a test of cure a single negative reaction is not sufficient In early syphilis a series of negative reactions extending over a period of two years is the minimum necessary to establish a cure

LAUGHLEN (Toronto) describes a simple and rapid test in which greater visibility is secured by the addition of a water insoluble stain which adheres to and colours the suspended particles of antigen but does not colour the liquid in which they are suspended Greater sensitivity and speed are effected by coarsening the suspended particles, for which purpose cholesterol is used Drops are placed on exposed slides so that the readings seen by the naked eye may be confirmed by the microscope if desired The reagent is difficult to prepare, but it is stable for at least some weeks Full details of technique are given in the original The test, it is stated, can be performed in a few minutes' time, needs very little equipment, is inexpensive, and can be done by any medical practitioner or technician without special training

Sigma Test —This test, introduced some years ago by Dreyer and Ward, consists in mixing various dilutions of patient's inactivated serum with antigen and incubating for 20 22 hours The antigen is a cholesterolized extract of calf's heart and is diluted with saline The reading of the results is carried out by noting the size of the flocculi and the dilution in which they occur and referring to a table which gives the results in numerals OSMOND (St Thomas's Hosp) describes it as a most valuable quantitative reaction it gives the results in units and is particularly useful in cases of late syphilis where it is desirable to gauge the progress of treatment It is not the most satisfactory qualitative test, but as a quantitative test it appears to have no equal In one of the cases described the sigma test showed 54 units, after ten injections it

fell to 22 2 A second course brought the figure down to 8 3, and a third course to 3 9 The patient showed no symptoms at any time and the W R was positive throughout

Kahn Test—This test has met with considerable favour in this country as well as in America where it originated It consists in setting out several tubes containing mixtures of antigen and serum in different proportions, with controls, after addition of saline solution the degree of flocculation is read off in terms varying from 'four plus' down to 'minus'

Kline Test—A microscopic slide precipitation test, based on the Kahn method, was introduced by Kline (Cleveland) in 1926, and since then has several times been modified by its introducer The test is applicable to blood serum or to cerebrospinal fluid

SCHMITZ (Berlin) records his experience with this test on 2100 specimens of serum and 187 spinal fluids, and concludes that in sensitivity and specificity it takes an intermediate position between the turbidity and the clarification tests of Meinicke

Meinicke Clarification Test (Klarungsreaktion M K R)—This is a modification of Meinicke's original turbidity test (Trubungs-reaktion M T R) and depends upon the clearing of an opaque mixture of serum and antigen With a strongly positive reaction the mixture, originally opaque, becomes clear, with a slightly positive it is opalescent, with a negative it remains turbid The results can be read with the naked eye A micro test on the same principle has also been introduced, and more recently a modification of the test known as M K R II

KOCH (Tubingen) has used the M K R in over 36,000 cases and expresses preference for the micro method on account of its rapidity It sometimes fails, especially in congenital and in late syphilis, in which cases other tests should be employed in addition In ordinary cases it gives from 98 to 99 per cent of correct results BATTISTINI (Parma) reports on the M K R II, which he has used in over 1200 cases of syphilis and other diseases In non-luetic cases it gave a positive result in only 0 17 per cent, while in syphilitic cases a positive result was obtained in 95 9 per cent BOAS reports over 1000 cases in which the results were very similar

Hinton Test—This test was introduced by Hinton (Boston) in 1927, and has since been modified and simplified by him It is based on the reaction between syphilitic serum and a special antigen Two extracts are employed, made respectively from muscle and from heart, and both are made up with cholesterol, glycerol, and saline A positive reaction is indicated by agglutination into clumps in the case of the muscle indicator, and the formation of a ring with the heart extract, with more or less complete clearing of the medium The test is said to be particularly valuable in determining the absence or persistence of infection when the W R has become negative as the result of treatment

HOLLANDER, SCHLESINGER, and SCHMITT (Pittsburg) have studied

the value of the Hinton test in some 3000 cases, in all of which the serum was subjected to four different tests. The Hinton proved to be more sensitive than the Wassermann or the Kahn. Of 655 definitely syphilitic patients, 643 gave a positive Hinton reaction, the next being the Kahn with 400 positive readings. Of 227 negative to other tests but positive to the Hinton, 208 were subsequently proved to be syphilitic. Of great clinical importance is the early appearance of the Hinton reaction, which precedes the Kahn and the Wassermann by three or four days.

CHEEVER (Boston) says that the Hinton test is particularly valuable in the latent and late stages of the disease where the Wassermann test is less reliable. False positives are fewer with the Hinton than with the other tests. In the detection of unsuspected syphilis in the presence of other conditions the Hinton test was found to be twice as efficacious as the Wassermann.

Arsphenamine Compounds.—Though arsphenamine ('salvarsan' or '606') is not official, two of its most generally used compounds are now included in the British Pharmacopoeia. *Neoarsphenamine*, or novarsenobenzene, is the compound originally known as neosalvarsan or '914' and occasionally referred to as 'NAB.' It is a yellow powder, soluble in water, and the dose by intravenous injection is 0·15 to 0·9 gm. *Sulpharsphenamine* represents the compounds known as sulfarsenol, kharsulphan, myosalvarsan, sulpho-stab, thio-sarmine, etc. It also is a yellow powder, soluble in water, and is given by subcutaneous or intramuscular injection in doses of 0·1 to 0·6 gm.

The British Pharmaceutical Codex, 1934, describes arsphenamine and silver-arsphenamine. *Arsphenamina*, or arsenobenzene, is a yellow powder, soluble in water. It is given only by intravenous injection. A slightly alkaline solution, containing the disodium salt, is employed. Arsphenamine has almost entirely given place to neoarsphenamine in therapeutics. *Arsphenamina Argentica*, or silver arsphenamine, is a brownish-black powder, soluble in water. It has about twice the spirochaeticidal value of arsphenamine, but is more toxic. It is given intravenously and is used chiefly in advanced cases. The dose is 0·1 to 0·6 gm.

Acetarsol (*Acetarsone*).—This is a 5-valent arsenical compound and is known commercially as stovarsol, kharophen, spirocid, etc. It is a white powder, almost insoluble in water, containing 27·2 per cent. of As. It is given by mouth in tablet form, the dose being 0·03 gm. (½ grain) for children, and 0·25 gm. (4 grains) for adults. Its chief application is in the treatment of malaria and amoebic dysentery, but it is occasionally used in syphilis, in which it seems to have some value, especially in children.

DAVIDSON and BIRT (Winnipeg) report on the use of acetarsol (stovarsol) in the treatment of congenital syphilis. A series of patients, of ages ranging from a few weeks to 15 years, were treated, and the results are compared with a series treated before the

introduction of this drug to the hospital Of the 'pre-stovarsol' group of twenty-seven, only six became Wassermann-negative after seven years' treatment, while of twenty-three treated with acetarsol fourteen became negative after two years The drug was given by mouth, beginning with one-quarter tablet (one grain) daily, increasing the frequency and the dose gradually to one tablet (4 grains) twice daily, the total being 56 tablets (14 gm) in 49 days, followed by a rest period of six weeks Three patients showed mild toxic symptoms, but otherwise the results were most satisfactory,

FAN (Shantung) describes seven cases of congenital syphilis in Chinese children similarly treated All showed complete healing with improvement in general health Syphilitic bone lesions also showed healing

MITCHELL (Montreal) also reports on its use in congenital syphilis The only real advantage, he says, over other forms of treatment is the oral method of administration This is very convenient for children, and secures the co-operation of parents which is so essential Results are satisfactory, toxic reactions are about as frequent as with arsphenamine, but appear to be less severe Caution is necessary with this drug as it is with other arsenicals

Mapharside — This recently introduced arsenical (Parke Davis) is described as the hemi-alcoholate of meta-amino para-hydroxyphenylarsine oxide hydrochloride Its formula is $HCl(NH_2)C_6H_3(OH)AsO \cdot \frac{1}{2}C_2H_5OH$, and it contains 29 per cent of trivalent arsenic It is specially recommended for the treatment of early syphilis, and is said to give less severe reactions than neo-arsphenamine It is a white powder, soluble in water, alcohol, acids, and alkalis The aqueous solution is acid to methyl red but alkaline to congo red The dose, intravenously, is 0 03 gm for women and 0 04 gm for men, gradually increased to a maximum of 0 06 gm The safe dosage is much lower than that of neo-arsphenamine In America it is called *Mapharsen*

GRUHZIT (Detroit) reports on its use in experimental syphilis A dose of one mg per kg of body-weight possesses higher therapeutic value than a dose of 10 mg /kg of neoarsphenamine, and the drug appears to be well tolerated A preliminary clinical report is presented by FOERSTER and associates (Univ of Wisconsin) Mapharside is given intravenously and the technique of its administration is as simple as that of neoarsphenamine Observations were made on eighty patients with early syphilis, no other treatment being employed Evidence of its action appeared promptly in all visible lesions, which healed rapidly Spirochaetes in open lesions disappeared usually in twenty-four hours The W R was reversed to negative in nearly all cases return to positive occurred in about half of the cases, in some of which it was associated with abnormal findings in the spinal fluid Clinical relapse occurred usually in cases receiving irregular or short periods of treatment Nitritoid reactions did not occur and the immediate toxic reactions were

chiefly mild gastro-intestinal disturbances: in properly adjusted doses the drug was well tolerated. Mapharside appears to be worthy of further investigation.

Neocryl (Crylarsan).—Under this name a new arsenical compound has been prepared in this country and is described by YORKE and MURGATROYD. Chemically it is sodium succinanilomethylamide-*p*-arsonate, and it is a white crystalline substance readily soluble in water. It is the result of an investigation extending over some years in which a large number of compounds were examined. Compared with tryparsamide in experimental animals it was found to be less toxic and more trypanocidal. In man it was found to be well tolerated in the same doses as tryparsamide, 2 to 4 gm. weekly, a course consisting of this amount weekly until 30-36 gm. had been given. Apart from very occasional nausea and vomiting, the only toxic signs observed were mild arsenical dermatitis in two patients and temporary jaundice in two or three very advanced cases of neurosyphilis after prolonged courses. Visual disturbances were not recorded, but their possibility should be kept in mind. Neocryl exerts the stimulating action associated with tryparsamide and other quinquevalent arsenicals. Unlike tryparsamide it exerts a definite action in primary, secondary, and tertiary syphilis. In primary syphilis it proved inadequate by itself, but combined with bismuth its results appeared to be more permanent. It has a very definite action on tertiary manifestations, the lesions disappearing completely in the majority of cases. In early neurosyphilis and in tabes it gave very satisfactory results. It also had a very definite action in a number of cases of Nigerian sleeping sickness.

Toxic Effects.—Further study has led to a better understanding of the toxic effects occasionally produced by the arsphenamine compounds, so that prophylaxis and treatment are now comparatively simple. The effects vary from simple gastro-intestinal symptoms and skin eruptions to severe reactions, jaundice, and blood dyscrasias.

The post-arsenical phenomenon known as 'Milian's ninth-day erythema' was referred to last year (PRESCRIBER, 1935, Aug., 255). It is a mild reaction occurring nine days after the first administration of arsphenamine. Several cases have recently been reported. FOSTER (Birkenhead) reports a typical case, which cleared up after two days' rest in hospital and did not recur under further arsenical treatment. GORDON (London) records two cases and shows that it differs from arsenical dermatitis, but that it appears to be due to the same cause, the difference depending upon the sensitiveness of the patient.

SANES and JORDAN (Buffalo) report two cases of non-fatal jaundice associated with arsphenamine treatment. In both cases an opportunity was presented for histological examination of the liver—in one the patient died from other causes and in the other material was obtained during an operation for suspected cholelithiasis. Neither spirochaetes nor bacteria were found in the hepatic tissue

and the lesions in both cases closely resembled those seen in fatal cases of arsphenamine jaundice Attention is directed to the necessity for regarding arsphenamine as contraindicated in patients with hepatic damage

Discussing the toxic hepatitis which occurs during arsenical treatment, APPEL and JANKELSON (Boston) show that recovery from this may be greatly facilitated by the use of sodium dehydrocholate, 10 c cm of a 5 per cent solution of this salt being added to the arsphenamine solution before injection If this is done, arsphenamine treatment may often be continued in the presence of jaundice

SWARTZ, TOLMAN, and LEVINE (Boston) report a case in which death followed the administration of bismarsen, an organic compound of arsenic and bismuth (see PRESCRIBER, 1934, Aug , 267) The patient had been under arsenical treatment for a time, and slight jaundice had developed Treatment was suspended until the jaundice had cleared, when it was resumed with bismarsen After the second injection the patient developed severe jaundice and died within twenty four hours Necropsy showed that fatty changes in the liver were not pronounced but that fat embolism of the lungs was widespread This was evidently the cause of death and it is attributed to the arsenical content of the drug

Dealing with the ocular reactions following arsphenamine treatment, SKIRBALL and THURMON (Boston) express the opinion that these are due to the toxic effects of arsenic The clinical syndrome consists of blurred vision and floating spots or flashes of light before the eyes If therapy is continued the haziness of the vitreous increases rapidly and becomes nebulous and cloudy to a point at which all details of the fundus are obscured The condition grows progressively worse, causing optic neuritis and possibly secondary optic atrophy If arsphenamine is discontinued early improvement of vision is rapid, and the fields of vision return to normal Further treatment during this complication may be carried on with iodides, bismuth, or mercury

Bismuth Therapy —The therapeutic value of bismuth preparations depends less on their metallic content than on their chemical constitution and physical properties, their rate of absorption and excretion, and their power of penetration The electrical charge carried by the bismuth ions has much to do with this last property a negatively charged ion penetrates into the cerebrospinal fluid, while a positively charged ion (as bismuth salicylate) does not

The preparations of bismuth at present in use in the treatment of syphilis may roughly be divided into three groups—water insoluble, water-soluble, and oil soluble or liposoluble

The water-insoluble preparations in the British Pharmacopoeia, 1932, are *Bismuthum Praecipitatum*, which is given in the form of *Injectio Bismuthi*, a 20 per cent watery suspension , also *Bismuthi Salicylas* (*Bismuthi Subsalicylas*, U S P), given intramuscularly as a 10 per cent suspension in olive oil, *Injectio Bismuthi Salicylatis*

Various preparations containing other insoluble salts such as oxychloride, hydrate, etc., are on the market. Another water-insoluble bismuth compound is *Quinine Bismuth Iodide*, which is much in favour on the Continent.

Of the water-soluble preparations the chief are the alkali bismuthyl tartrates, an example of which is found in *Bismuthi et Sodii Tartras* (neutral), B.P.C. The equivalent of this in the United States Pharmacopoeia, 1936, is *Bismuthi et Potassii Tartras*, which contains 70 to 75 per cent. of Bi_2O_3; the dose by injection is 0·15 gm. (2½ grains). A product recently introduced in America is *Iodobismitol*, a solution of sodium bismuth iodide in ethylene glycol. It is given by intramuscular injection in doses of 2 c.cm. every three days, and is said to be well absorbed and to be excreted fairly rapidly. The bismuth in this compound is electro-negative.

Quite recently a modification of iodobismitol containing saligenin has been described by HANZLIK, BARNET, and RICHARDSON (San Francisco). This preparation contains sodium bismuth iodide, 6 per cent., sodium iodide, 12 per cent., and saligenin, 4 per cent., in propylene glycol. It is administered by the same route and in the same dose as iodobismitol, the saligenin acting as a non-toxic and non-irritant local analgesic, while the propylene glycol avoids all possibility of systemic or cumulative toxicity sometimes attributed to ethylene glycol. Comparative observations on over 1000 clinical patients indicated a better tolerance than was shown with iodobismitol. [Saligenin, or salicyl alcohol, the local analgesic, was described in our issue of April last, p. 133.]

The liposoluble preparations are of comparatively recent introduction. *Bivatol* consists of basic bismuth α-carboxethyl-β-methyl-nonoate dissolved in a fatty vehicle, and contains 0·035 gm. of bismuth in one c.cm. *Bi-liposol* is a solution in oil of bismuth camphocarbonate (or camphocarboxylate), containing 0·04 gm. bismuth per c.cm. In other countries bi-liposol is marketed under a variety of trade-names; in America it is called *Bismo-cymol*. Unfortunately the name 'biliposol' (without a hyphen) has been adopted by the American Medical Association for bismuth α-carboxethyl-β-methyl-nonoate, the compound known everywhere else as 'bivatol.' This has already led to some confusion. Another oil-soluble product is *Neo-Olesal*, or bismuth dimethyl-endo-methylene-hexahydrobenzoate, 10 per cent. solution in oil; it contains 30 per cent. of bismuth. The advantage of the oil-soluble preparations is that they form deposits which are absorbed slowly, though more rapidly than the metal itself.

Toxic Effects.—SÄUFERLIN describes the case of a man with primary syphilis and a positive W.R. in whom bismuth therapy caused the development of a linear haemorrhagic lesion following the course of the left saphenous vein. He thinks that the haemorrhage was due to an increased permeability of the vein resulting from a syphilitic inflammation plus the laying down of metallic bismuth in

the vessel wall Experiments with animals showed that bismuth has an affinity for inflammatory tissue, especially for tissue which is the site of a syphilitic inflammation

Discussing the ulcerative stomatitis following the therapeutic use of bismuth and mercury, AKERS (Hot Springs, Ark) shows that this may be prevented mainly by cleanliness of the mouth Complete oral prophylaxis is a necessity removal of bad teeth and insanitary fittings and temporary filling of large cavities For treatment, pockets and ulcerated surfaces should be cleansed with a mixture of equal parts of tinctures of aconite and iodine, this precipitates bismuth or mercury as insoluble iodide Sodium bicarbonate acts as a neutralizing agent on the bacterial acid present in the mouth A saturated solution is applied to the gums from a compressed air syringe with sufficient pressure to remove the precipitate and gangrenous tissue, and patients are instructed to use the same drug freely to rub the gums brush the teeth, and rinse the mouth

Mercury.—In a series of studies on the action of mercury, SOLLMAN, SCHREIBER, and COLE (Cleveland, Ohio) now report on the excretion of that metal They find that to be effective the mercury must be in the body in a diffusible condition when fixed in the tissues it has no therapeutic value The urinary excretion serves as an indicator of the diffusible mercury all effective methods show continuously cumulative excretion Effective treatments secure a daily urinary excretion of 0 8 to 1 0 mg of mercury at the end of the fourth week these include massive inunctions, grey powder orally, and intramuscular mercury oil—this last is liable to be cumulative Oral mercurous iodide has a high rate of excretion and is liable to cause stomatitis

In a later article SOLLMAN, COLE, and SCHREIBER conclude the report of their investigations on mercurial inunctions (see PRESCRIBER, 1933, Aug , 264) The most effective inunction, as judged by the urinary excretion, is an ointment of oleate of mercury made with vanishing cream , after that comes a 50 per cent ointment of metallic mercury, the vehicle being immaterial Colloidal mercury is absorbed unequally and its effect is poor

Other Remedies —Discussing the employment of iodine in the treatment of syphilis, BURKE (Salford) maintains that it plays an important part in every stage of the disease It prevents the formation of fibrous tissue in acute syphilis, and in the chronic stage it causes its absorption It should invariably be given in association with arsphenamine or bismuth therapy Intravenous injection of colloidal iodine is very effective

Vaccine Therapy — HILGERMANN (Landsberg) expresses the opinion that the efficacy of chemotherapeutic agents in syphilis is due not so much to sterilization as to immunization By killing off the pathogenic organisms such agents liberate the toxins and thus start an active immunization The action of arsphenamine is

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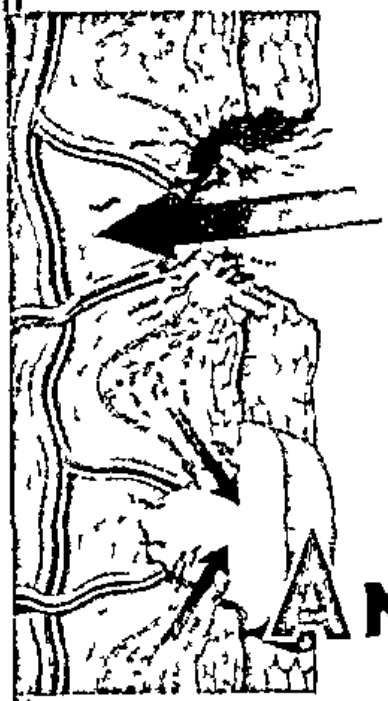
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Neurosyphilis.—Dealing generally with the treatment of syphilis of the nervous system, HOLMES (London) groups cases with established lesions into three main types: (1) *meningeal*, in which the predominant lesion is acute or chronic infiltration by gummatous cells of the membranes of the brain or spinal cord; (2) *vascular*, in which endarteritis may reduce the blood flow to the nervous tissue within the distribution of the vessel; (3) *systemic or parenchymatous syphilis*, characterized by the predominant affection of neural tissues. Each of these groups requires special consideration before treatment is instituted. The meningeal type is best treated by intravenous neoarsphenamine, with possibly bismuth at the same time. Lesions of vascular origin are the least amenable to treatment. Arsenicals are rarely advisable: iodides and bismuth are safer and probably equally effective. In chronic tabes the intramuscular administration of bismuth is the most useful treatment: courses may be alternated with inunctions of mercury. For general paralysis tryparsamide and acetarsol have been largely used, but are apt to produce optic atrophy. The introduction of malaria therapy has, however, revolutionized the treatment of general paralysis: it should be followed by energetic arsenical treatment for at least two years.

HOSSACK and PETERSON (Winnipeg) emphasize the importance of examination of the spinal fluid, for it is there that changes first occur. Such changes as increased cell count, increase in globulin, and positive colloidal or Wassermann reactions may long antedate the appearance of definite signs. The first evidences of neurosyphilis are to be found not in the patient but in the test-tube, and search for them must never be omitted. When gross involvement of the nervous system occurs the physician may be confronted with any syndrome: that of neurosyphilis is of infinite variety and rarely shows a clear-cut picture. Treatment gives best results in the asymptomatic cases. It should begin with eight to twelve malarial chills; after a few weeks' rest a course of eight to ten weeks' treatment with small doses of neoarsphenamine and full doses of bismuth and iodides may be given, followed by the quinquevalent arsenicals. A re-check of the spinal fluid in six months will probably show that the danger has passed.

Tryparsamide (*Tryparsone*).—This is a quinquevalent organic arsenical compound, sodium *N*-phenylglycineamide-*p*-arsonate, and contains about 25 per cent. of arsenic. It is a colourless crystalline powder, freely soluble in water, forming a neutral solution. Its dose

ranges from 0 5 to 3 gm (8 to 45 grains) according to the purpose for which it is required, it should not exceed as a rule 0 04 to 0 05 gm per kg body weight It is given only by injection, subcutaneous intramuscular, or intravenous—usually the last—never by mouth, and not more often than once a week On account of its tendency to produce optic atrophy, great care must be observed in its administration

SOLOMON and EPSTEIN (Boston) present a study of eighty one cases of dementia paralytica treated with tryparsamide and observed over periods varying from three to fifteen years In 42 per cent the disease was clinically arrested and in 37 5 per cent the spinal fluid became normal These results do not differ materially from those obtained with malaria therapy In some cases which failed to respond to tryparsamide subsequent malaria treatment was of definite benefit

Fever Therapy—The employment of malaria and other methods of inducing pyrexia is being increasingly recognized especially in the treatment of general paralysis Malaria is generally regarded as giving the best results but in cases in which it is impracticable or undesirable such methods as intravenous injection of typhoid vaccine, intramuscular injection of colloidal sulphur preparations, diathermy, etc, may be employed The general opinion regarding these methods is that they are safer than malaria, but therapeutically less effective

Malaria—In this method the patient is inoculated with benign tertian malaria either directly from mosquitoes or, more usually, by injection of blood drawn from a malaria patient When the blood is injected subcutaneously the incubation period varies from fourteen to twenty one days, when the intravenous route is employed the average period is seven days The malaria runs its usual course and the patient is allowed to have as many rigors as he can stand—usually from eight to twelve are sufficient He must have the most careful nursing and continual supervision After a sufficient number of rigors the malaria is easily cured by the administration of quinine or plasmoquine compound With inoculated malaria there is no fear of malarial relapses or chronic malarial infection Convalescence is usually rapid Complete return to normal, so that the patient can resume his usual work, is obtained in about 35 per cent of all cases The mortality rate is low

WAGNER JAUREGG (Vienna), the discoverer of malaria therapy, offers an explanation of the action of malaria in general paralysis Malaria appears to have a direct action on the brain of the paralytic It exerts a focal reaction on the nervous system indicated by an increase of the amino acids in the cerebrospinal fluid Malaria treatment has a definite action on the reticulo endothelial system The difference between malaria and other methods of inducing pyrexia is that in malaria the leucocyte change is preponderatingly leucopenic, whereas in the other forms there is a considerable

increase of leucocytes—this leucocytosis has a preponderatingly neutrophilic character. The destruction of erythrocytes is characteristic only of malaria.

Although malaria gives the best results in general paralysis, other conditions have been benefited by its application. RUDOLF (Bristol) refers to its use in tabes, schizophrenia, manic depressive psychoses, disseminated sclerosis, and chronic gonorrhoea, in all of which it has been shown to be of benefit. MENZIES (Saint John, N.B.) believes that its value, next to general paralysis, lies in the treatment of tabes, and describes two cases in which it effected great improvement. SOLOMON and EPSTEIN (Boston) report their results in 173 cases of general paralysis; good recovery with normal spinal fluid was obtained in 36 per cent. and improvement in 27 per cent.

Some years ago (1932) it was shown by Knowles and Das Gupta, of Calcutta, that ape malaria caused by *Plasmodium knowlesi* could be transmitted to man. Certain disadvantages attendant on the induction of benign tertian malaria (*P. vivax*) led VAN ROOYEN and PILE (Edinburgh) to try the effect of ape malaria in general paralysis. Infection by this parasite has an incubation period of eight or nine days or less and is followed by pyrexia of the quotidian type. Such infection has been used successfully in general paralysis, the treatment consisting of eight rigors. It was found that atebrin, while it acts specifically in the monkey, failed to diminish the pyrexia in human infection, but quinine dihydrochloride exerted an immediate action, an intramuscular injection of 7½ grains reducing the fever within an hour. The advantages of this method are: a short incubation period; gentle onset of pyrexia and gradual increase of temperature with each quotidian rigor; the rapid termination of fever by quinine; the freedom of the monkey's blood from the possibility of syphilitic infection. The viability of *P. knowlesi* at low temperatures renders it possible to store infected blood in an ice-chest and use it when required. A recent report by CHOPRA and DAS GUPTA fully confirms the advantages of this treatment, although they add that a larger number of cases will have to be so treated before its value can be properly judged.

Artificial Pyrexia.—NEYMANN (*Chicago*) speaks highly of diathermy or electropyrexia, which he finds of great value in tabes, general paresis, tabo-paresis, and cerebrospinal syphilis. His technique is to raise the temperature above 103·5° F. for six hours, then to increase to 105·8° for two hours. Treatments are given twice weekly and the approximate number of treatments required is twenty. Neymann has treated seven cases of syphilitic optic atrophy, a minimum of twenty treatments being given to each patient, with temperatures ranging above 105·8° for four hours, while the patients' treatment lasted for at least eight hours with a temperature above 103·5°. This is the maximum upper limit of safety.

NATTRASS and EVANS (Newcastle-upon-Tyne) report the use of

short-wave therapy in fifteen cases of dementia paralytica, and report that the results compare favourably with those of malaria therapy, while the method is safer and capable of precise control.

SIMPSON (Dayton, Ohio), whose preliminary report was mentioned last year (PRESCRIBER, 1935, Aug., 261), now describes fully the use of the 'Kettering hypertherm,' a cabinet in which it is possible to elevate the patient's temperature rapidly and to maintain it at the desired level for an extended period. During four years 383 patients have received 2844 treatments without any serious ill-effects. Combined with chemotherapy it is of great value in early syphilis, particularly where chemotherapy appears to be inadequate. In the various forms of neurosyphilis the results are at least comparable with those obtained from malaria, while hospitalization is not required. At the International Congress of Physical Medicine held in London recently, SIMPSON stated that of 27 cases of G.P.I., 21 had obtained complete clinical remission and four showed improvement; injections of arsenic and bismuth had been given prior to each of ten weekly sessions of pyrexia. The course was followed by a further twenty weekly injections.

EPSTEIN, SOLOMON, and KOPP (Boston) review a series of thirty-three cases treated by diathermy in two years. Of these eight are improved and working, seven are improved but not working, four are improved but still in hospital, four are unimproved, and ten have died. Of the fifteen improved patients, eight now have normal spinal fluids. Their conclusion is that fever produced by diathermy has some value in general paralysis but is not so effective as malaria.

Reviewing the various methods employed for the production of therapeutic pyrexia, WALINSKI (Berlin) divides these methods into four groups: (1) non-microbic preparations, (2) microbic products, (3) bacterial diseases, as malaria, (4) physical methods. In the first group are compounds of complex proteins: these are not powerful enough to replace malaria in the treatment of general paralysis, although they are serviceable in other conditions. Vaccines prepared from killed bacteria should not be used in general paralysis unless malaria cannot be employed. Malaria is the best treatment of all, although rat-bite fever has been found by some to be equally effective and more convenient—the spirillum can be grown on culture. The success of physical pyrexia has been remarkable, but the method is not without danger Walinski describes a means of producing pyrexia by injection of hypertonic saline followed by a warm bath and hot packs. An intravenous injection of 10 c cm. of 10 to 20 per cent. sodium chloride solution is first given, then the patient is put in a bath at 99 to 101° F., gradually raised to about 107°. After this the fall of temperature is checked by a hot pack of flannel and wool. The method has been used in tabes, general paralysis, and cerebrospinal syphilis with good results, but the percentage of improvement (28) is misleading as it includes several nonsyphilitic conditions. In general paralysis alone the results were scarcely as good as the average results from malaria.

Holmes-Adie Syndrome—This benign clinical entity simulating neurosyphilis is described by BRAMWELL (Edinburgh) The condition is characterized by immobile pupils and by diminution of some of the deep reflexes It is more common in women and usually appears in early adult life Its pathology is unknown The syndrome is not the precursor of progressive organic disease, and is not related to syphilis, although it has often been erroneously diagnosed as neurosyphilis

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REVIEWS OF BOOKS.

A Handbook of Tropical Therapeutics By R N Chopra, *C.I E*, M D, M R C P, Bt-Col I M S, Professor of Pharmacology, School of Tropical Medicine, Calcutta Pp 1748 (Art Press, Calcutta Rs 25)

This may fittingly be described as a monumental work In its seventeen hundred and odd pages it appears to miss nothing that may be of service to the student of tropical medicine or to the physician practising in a tropical country The author is an acknowledged authority on tropical medicine and much of his own work will be found in the book The main portion is divided into six parts the opening section—about 250 pages—deals with therapy in general, including drugs, chemotherapy, physiotherapy, diet, pyrexia, hypnotics and tonics The next four parts deal at length with the various groups of tropical diseases and their treatment, while the concluding section is devoted to diseases of the skin The Appendices contain a vast amount of miscellaneous information, while a well arranged and not too elaborate index appears at the end The book is well bound—a necessity for a work of its bulk, but a little more care in proof reading would have avoided the long list of 'errata' (which by the way is not complete) given at the beginning of the book That of course will be remedied in future editions The book fills a place hitherto vacant and will certainly come to be recognized as a standard reference work for physicians, particularly in India

Confessions of a Ghost Hunter By Harry Price Pp 396 (Putnam 10s 6d)

The author is the founder and a director of the National Laboratory of Psychical Research and has written a baker's dozen of books on psychic phenomena and kindred subjects His specialism cannot therefore be questioned In the present volume although he wears an air of detachment it is pretty clear that his scepticism is uppermost—a consideration satisfying to the readers of a journal such as this Perhaps the most interesting thing in the book (because one hears so little about it) is the *poltergeist* phenomenon in plain English the haunting of houses by invisible ghosts Crockery falls off shelves with a loud bang the fire is raked out of the kitchen grate at midnight with danger to life and property, footsteps are heard doors are opened and closed, articles are overturned or placed in new positions—all without visual or attributable agency! There is much also about mediums and spiritualistic happenings, fire walkers, the Indian rope trick, telepathy, the talking mongoose in the Isle of Man, Abram's Magic Box, and much else—and the reader is left wondering whether the explanation is new phenomena or just old fashioned credulity The moral of this brightly written book (not, we think, completely innocent of leg pulling) is this what evidence there is is at second hand, hearsay evidence which is no evidence at all The genuine sceptic seems always debarred from the privilege of first hand proof, he seems to vitiate the atmosphere congenial to ghostly happenings One feels that until some psychic occurrence comes one's own way one may legitimately have recourse to the salt-cellar R C O

In CHANGE OF LIFE IN MEN AND WOMEN (Putnam, 6s) Dr Marie Stopes has added another to her useful series of books on sex hygiene Unlike most works on the subject, this book gives some attention to the male climacteric, the importance of which is usually underestimated This is dealt with in the earlier chapters, the rest of the book being devoted to the female aspect Dr Stopes rightly expresses preference for the term 'change of life' or 'climacteric' to 'menopause,' as cessation of menstruation is merely an incident in the change Dr Stopes as usual writes fearlessly—a little restraint here and there would improve her style and possibly make it more convincing—but she writes as she feels and she is obviously sincere *Her book is full of sound advice and should help to* a better knowledge of a rather neglected subject

Under the title of MORAL PLAYS (Constable, 7s 6d) Mr James Bridie (Dr H O Mavor) has published three of his recent plays with a quasi-Shavian preface entitled 'The Anatomy of Failure' In this he explains how of the three plays here presented, *Marriage is no Joke* ran for five nights; *Mary Read* scored one hundred performances but caused the producers a loss amounting to five figures (that seems tremendous—surely some of the figures must have been shillings and pence!), *The Black Eye* died in the sixties With considerable shrewdness he conducts a post mortem on these failures, for which the audiences rather than the plays were responsible Plays that read well—and Mr Bridie's plays all read exceedingly well—don't always act well, and even when well acted (as *Mary Read* certainly was) they don't always appeal to an audience out for an evening's amusement If Mr Bridie can profit by this experience the failure of his three plays will not do him any harm

SURGEONS' HALL is the title of a new journal issued by the School of Medicine of the Royal Colleges of Physicians and Surgeons of Edinburgh. It contains a number of interesting articles by licentiates of the school and others there are numerous illustrations, and the lighter side is not neglected The journal is to be issued three times a year and the subscription is three shillings per annum, post free to any part of the world It should have a wide circulation among old students

THE COMMON COLD AND INFLUENZA by J E R McDonagh F R C S (Heinemann, 12s 6d), is the subject of the 'Nature of Disease Annual Reports' for 1934 and 1935 Here the author, as usual tackles this important problem from a new angle showing the relationship of these prevalent complaints to the rest of medicine The book runs to 152 pages and the author's main thesis of the similarity of causes in different diseases is logically applied to the problem here presented

The Institute of Ray Therapy, Camden Road London N W 1, has issued its SIXTH ANNUAL REPORT The object of the Institute is to provide actinotherapeutic and electrical treatment free or at moderate charges to persons of small means The Institute is doing good work and its finances appear to be in a sound condition, but it is not self supporting and relies largely on outside assistance The account of its work as given in the Report makes interesting reading

A useful little DICTIONARY OF DIETARIES has been issued by Energen Foods Co Ltd, Willesden, London, N 10 It is issued free to members of the medical profession

CORRECTION—In our issue of July, p 247, Fortamin is stated to contain calcium glycerophosphate This is incorrect it should be sodium glycerophosphate

On account of the extra space occupied by the Review on Syphilis, several other features have been held over till next issue

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MEDICINE IN THE TROPICS.

THE present issue, being devoted in large measure to the study of malaria, affords an appropriate occasion for reference to tropical medicine generally. To make the tropics safe for the white man and more comfortable for the native is a task in which the British nation has always taken a prominent part. Sir Patrick Manson has been styled the 'Father of Tropical Medicine,' and as our overseas dominions cover a very large territory it was only right that this country should take a leading position in such work. During comparatively recent years other nations have acquired an interest in tropical diseases, and workers from many countries have followed the investigations of Manson, Ross, Bruce, and others, with benefit to the world as a whole.

All this work, which during recent years has increased enormously, would have conferred more lasting benefit had the acquired knowledge been better co-ordinated and had the means of obtaining it been better organized. It is gratifying, therefore, to learn that the Medical Research Council has decided, in consultation with the Colonial Office, to establish a Tropical Medical Research Committee for the purpose of advising and directing such investigations as the Council may promote. When this announcement was made some months ago it was stated that the new Committee would be a purely scientific body and would include representatives of the Colonial Office and of the Schools of Tropical Medicine in London and Liverpool with such other experts as might appear advisable. The original membership includes some dozen names already

well known in this branch of medicine. The Medical Research Council has never actually neglected the study of tropical medicine, but hitherto it has been unable to assist investigations in the tropics except on isolated occasions although it has regularly made grants for such work at home. The establishment of this committee will enable the Council to extend its activities and to deal with work abroad.

Among the problems of tropical medicine malaria undoubtedly occupies a leading position. Its wide prevalence causes an appalling amount of sickness and mortality and organized prevention is a necessity for the prosperity of a community and even for its very existence. The disease is the enemy of all enterprise and under its thrall whole districts become derelict. Fortunately the causes and transmission of malaria are well understood, thanks mainly to the magnificent work of Manson and Ross, and the means for its prevention are within grasp. Yet in spite of all this knowledge, and in spite of the weapons at disposal, the disease still plays unexpected tricks that baffle the best brains to circumvent. In the light of present knowledge the epidemic in Ceylon ought never to have occurred, yet it did occur and took a toll of 80,000 lives. Much can yet be done in regard to the prevention and treatment of malaria, as our review in this issue indicates.

While dealing with this subject it is fitting that we should make reference to the passing of one who has done much to promote medical research and whose efforts have not neglected tropical medicine. The name of Sir Henry S. Wellcome will always be associated with the research laboratories in London and in Egypt which bear his name, and whence much work of a most valuable nature has emanated. An American by birth, and fired with the enthusiasm and self-confidence characteristic of his countrymen, he became a British subject in 1910. He showed a particular penchant for medical history and for the organization of research, a dual hobby which his ample means enabled him to indulge freely. The Wellcome Research Institution in London is a permanent memorial to his enterprise, while the Wellcome Tropical Research Laboratories at Khartoum have been the scene of many important and useful investigations into the endemic diseases of tropical Africa. Sir Henry died on July 25 at the age of 82, and he has left a legacy for which medical science will long have reason to be grateful.

THE TREATMENT OF MALARIA.

A Year's Progress.

AN official Report has been issued by the GOVERNMENT OF CEYLON dealing with the epidemic which occurred in the island during 1934-35. In our review last year (PRESCRIBER, 1935, Sept., 271) all the information then available was given. The official Report is very full and contains much detail which need not be repeated here. The first volume is mainly a statement of facts and figures: discussion has been kept at a minimum and deductions as a rule are avoided. The other volume (Paper xxiii) is by Colonel C. A. Gill, I.M.S., who was invited to visit the island for several months as expert adviser on malaria.

The epidemic was the greatest pestilence in the recorded history of the island: it destroyed 80,000 lives in seven months. Almost all parts of Ceylon were affected, but in a region embracing one quarter of its area and one third of the population the violence of the epidemic was extreme and scarcely a single individual escaped. Prior to the epidemic scarcity and famine, consequent upon a prolonged drought, prevailed in many parts of the island. Colonel Gill arrived in Ceylon in April 1935 when the epidemic was definitely on the wane, but this did not affect his work, which was to review the epidemic and consider its possible consequences, to review the antimalaria work of Ceylon during the past twelve years, to define future policy, and to formulate the scope and powers of an Anti-Mosquito Ordinance. Colonel Gill's Report contains 46 foolscap pages and is supplemented with numerous maps, charts, and illustrations. The various factors concerned in such epidemics are reviewed in detail, and while Colonel Gill admits there is no royal road to malaria control he outlines a policy which should be effective in preventing such epidemics in the future. The Report is concerned more with control than with treatment, the only reference to the latter being certain recommendations regarding the standardization of the formula for quinine stock mixture. Those interested should study the Report carefully. It is published by the Government Record Office, Colombo, at Rs. 4.50 for the first volume and Rs. 3 for Colonel Gill's Report.

As the result of a study of induced malaria by JAMES, NICOL, and SHUTE, it is concluded that the epidemic in Ceylon manifested itself in two waves, the major wave beginning in October and the secondary wave in the following April. *Plasmodium vivax* played a considerable part in the primary wave, the secondary wave being due to recurrences together with a fresh prevalence of the insect vector. James advances reasons for assuming that the onset was gradual, and not sudden as suggested in Gill's Report.

A case of congenital malaria, which is rare, is reported by TANNER and HEWLETT (London). The infant was the second born of twins,

the first child being unaffected. The parents were a Bengali and an Englishwoman; the mother had suffered from malaria in India and the children were born in London. It is thought that premature placental separation was the cause of transmission of the infection. The malaria yielded to treatment with atebrin.

Discussing the occurrence of malaria during pregnancy, WICKRAMASURIYA (Colombo) reports six cases in which the placental barrier was broken down and the child became infected *in utero*. The factors which influence transplacental infection are (1) the type of infection, in all cases malignant tertian (*P. falciparum*), (2) damage to the placenta, and (3) the efficacy of the treatment employed. Quinine in therapeutic doses (5 to 10 grains) does not act as an oxytocic; on the contrary, by rapidly controlling the infection and reducing the temperature it prevents premature interruption of pregnancy and intra-uterine foetal death. Atebrin is a useful drug, but its action is less rapid and in pregnancy it takes only second place. It is contraindicated in patients with toxaemia of pregnancy.

It is generally believed that tertian malaria transmitted by direct inoculation is easily cured by quinine, but several cases of recurrence have been recorded. PETERSEN (St Peter, Minn.) describes eleven cases, out of a total of over 200, in which recurrences took place *after malaria therapy followed by quinine treatment. Reinfection* was ruled out. Petersen thinks that a systematic research for the plasmodium in all malaria-treated patients will reveal a number of unsuspected recurrences.

THOMAS, KEYS, and DYKE (Wolverhampton) report a case of accidental transmission of malaria by blood transfusion. The donor, a brother-in-law of the patient, had served in India but had not had malaria while there, though he had suffered from several mild shivering attacks since his return. It is concluded that anyone who has resided in malarial regions is a potential carrier of the parasites, and that the use of such persons as donors is fraught with risk to the recipient. A very similar case is recorded by CADHAM (Winnipeg); the donor was the patient's father, who had travelled in countries where malaria was endemic. He had no recollection of ever having an attack, but his blood showed the presence of *Plasmodium malariae*.

The question of immunity has been studied by CHOPRA and MUKHERJEE (Calcutta). A survey of previous work shows that while specific antibodies have not been definitely demonstrated, indirect evidence of their existence has been obtained. The mechanism of phagocytosis is believed to be due to a reduction of electrical charge on red cells. Both red and white cells being negatively charged, ordinarily the forces of electrical repulsion prevent a white cell from coming near a red cell, but when this red cell is infected its electrical charge is diminished and the approach of the two becomes a possibility. Recent experiments have shown that the charge on the infected cells is dependent on the stage of growth of the parasite within the cell, while the relationship between the

electrical charge and phagocytosis is governed by the laws of collision between charged particles as in colloids. Biochemical changes in the plasma are now being studied, and it is hoped that before long it will be possible to imitate these changes artificially and thus to induce immunity to the disease.

Diagnosis.—The serum-flocculation test introduced by Henry in 1928 has been described in previous reviews. At first a salt of iron, later melanin pigment from ox choroid, was used as the antigen, this being incubated with the patient's serum and the results read as in other serological tests. In the modification by Greig (Edinburgh) the antigen is melanin derived from human hair by hydrolysis with hydrochloric acid. In benign tertian malaria the reaction appears from five to seven days after infection, although no parasites are visible and the patient is afebrile.

Considerable controversy has arisen regarding the technique of this reaction. Some hold that the precipitate, being a globulin, is formed with distilled water alone and that melanin acts solely as an indicator. CHORINE and KOECHLIN recommend that the test be carried out with distilled water only, while PRUDHOMME recommends the use of a suspension of carmine as an indicator. BENHAMOU and GILLE advise the addition of cholesterol; this does not increase the flocculation but adds to the opacity by forming a precipitate of its own. HENRY, on the other hand, maintains that melanin plays a part in the reaction, the precipitate with distilled water being of a different nature. TRENSZ supports Henry, holding that the flocculation with melanin is due to a special euglobulin present only in malarial serum, and that the water precipitate is not specific.

COSTADONI examined the serum of 184 patients, including persons with malaria, persons who had had malaria, persons in sound health, and those suffering from other diseases. In all the malaria cases the reaction was positive. In those who had had malaria some were positive, some doubtful, and others negative—these last were regarded as cured. In diseases other than malaria, several with syphilis reacted positively, as also did some cases of haemolytic jaundice, Weil's disease, and cirrhosis of the liver. THIODET and RIBÈRE have obtained positive reactions in cases of pernicious anaemia, duodenal ulcer, and other conditions associated with anaemia; they regard the test as non-specific.

The appearance of the reaction in non-malarial cases is discussed by HENRY. In addition to those already mentioned, positive reactions have been reported in cases of trypanosomiasis, typhus, and kala-azar. Henry thinks that the reagents have certain properties of a colloidal nature which occasionally obscure the reaction, but this does not vitiate the specific nature of the test in human malaria.

BRANDT and HORN employed Henry's test in a number of cases of induced malaria used in the treatment of general paralysis. All the cases gave a positive reaction during malaria treatment and became negative on recovery from the malaria.

Cinchona Alkaloids —The mixture of cinchona alkaloids recognized by the British Pharmacopoeia as *Totaquina* or totaquine contains 70 per cent of crystallizable alkaloids from various species of *Cinchona*, one-fifth of which must be quinine The term *Quinetum* is not official and refers to a preparation consisting of quinine cinchonidine, and cinchonine in equal proportions Two types of totaquine are known, type I being the total alkaloids of *C succirubra* while type II is prepared from *C ledgeriana* residues with the addition of sufficient quinine to bring it to specification Type I is likely to have a higher quinine and a lower cinchonine content

The relative clinical efficacy of totaquine and quinine is discussed by HICKS and CHAND Adult male prisoners in Lahore who were suffering from malaria were treated with both drugs, including the two types of totaquine, according to the method recommended by the League of Nations In benign and malignant tertian malaria there was no distinct difference in efficacy between quinine and the two types of totaquine in causing disappearance of parasites and fever, all three drugs were well absorbed, and no significant difference in toxicity could be detected The choice of drug rests mainly on its cost

Research on modifications of the cinchona alkaloids still proceeds Last year reference was made to apoquinine, and since then GOODSON (Wellcome Research Labs) has reported on the chloro dihydro bases Two chlorodihydroquines have been tested for antimalarial activity in bird malaria and found to be about as active as quinine and a little less active than dihydroquinine This proves that chlorine in the alpha position in the side chain does not affect the antimalarial action

Plasmoquine and Atebrin —These synthetic products are now well established as remedies for malaria Plasmoquine is a salt of N-diethyl amino isopentyl 8 amino 6-methoxyquinoline It is a tasteless, light yellow powder, only very slightly soluble in water, and is issued in tablet form in three varieties *Plasmoquine Simplex* (0 01 and 0 02 gm), *Plasmoquine Compound* (plasmoquine 0 01 gm, quinine sulphate 0 125 gm), *Quino Plasmoquine* or *Quinoplasmine* (plasmoquine 0 01 gm, quinine 0 3 gm)

Plasmoquine simplex is recommended in cases of blackwater fever and quinine idiosyncrasy, plasmoquine compound is the form most generally employed in the treatment of malaria, quino plasmoquine contains a larger dose of quinine and is designed specially for prophylaxis The destructive action of plasmoquine is restricted to infection by *Plasmodium vivax* (benign tertian) in all its phases and while it has no action on the schizonts of *P falciparum* (subtertian) it has a definite action on the crescentic gametocytes of this organism For the treatment of benign tertian plasmoquine compound is most suitable the small dose being quite sufficient if supplemented with quinine In subtertian it is not curative, but its action on the gameto cytes has led to its employment as an antigametocyte The adminis-

tration of plasmoquine may be followed by certain untoward symptoms, such as colic, respiratory difficulty, and cyanosis, and for this reason it should be given only under close supervision.

Atebrin is an acridine derivative and occurs as a yellow powder. It is issued in two forms: atebrin tablets for oral administration and a soluble form called 'atebrin for injection.' The tablets contain 0·1 gm. of the dihydrochloride of 2-methoxy-6-chlor-9-α-diethylamino-8-pentylamino-acridine. Atebrin for injection is the dimethanesulphonate of the same base: during its trial stage it was known as 'atebrin-musonat' and it is still frequently referred to under that name.[1] It is issued as dry powder in ampoules containing 0·125 gm., the equivalent of 0·1 gm. of atebrin. The contents of an ampoule are dissolved in 3 c.cm. of water for intramuscular or intravenous injection. Both forms are used for the same purposes and in equivalent dosage.

Unlike plasmoquine, atebrin acts on the asexual forms of the parasites, in which respect it resembles quinine. As atebrin is more effective than plasmoquine in destroying the ring forms, the formation of crescents may be combated by a combination of the two drugs. The usual dose of atebrin is 0·1 gm. three times a day; in subtertian it is combined with 0·01 gm. of plasmoquine. Atebrin for injection (atebrin-musonat) is given in doses of 0·125 gm. dissolved in 3 c.cm. of water; stronger concentrations are apt to cause local irritation.

The toxicity of atebrin is low. In some cases a yellow pigmentation of the skin and conjunctiva is noticed, but this is due to the acridine content and is not the result of liver damage. The urine should be examined daily during treatment, as absence indicates possible accumulation in the system, which may give rise to the yellow coloration referred to. A simple test is to heat the urine with sulphuric acid in a test-tube, when the presence of atebrin is indicated by a characteristic yellow colour. A more delicate test is to render the urine alkaline, extract it with ether, evaporate the ether, and dissolve the residue in strong sulphuric acid, when a yellow fluorescent solution will result if atebrin is present.

A comparative study of the action of atebrin and of atebrin-plasmoquine combination is reported by CHOPRA, GUPTA, and SEN (Calcutta). A small series of cases was treated with atebrin alone and with a combination of atebrin (0·1 gm.) and plasmoquine (0·0033 gm.). In cases of benign tertian and quartan malaria the combination was not more effective than atebrin alone, but in cases of malignant tertian infection the combination proved more effective and the parasites disappeared more rapidly. In all forms of infection the relapse rate was definitely lower with the combined drugs, but the combination was more toxic than atebrin alone. SECKINGER (Altanta, Ga.) reports trials with atebrin and plasmoquine in a

1. The affix 'musonat' is a fancy term coined in the German laboratories for temporary purposes. The salt is not a 'musonate': there is no such thing as musonic acid.

highly malarious area Atebrin was found to be particularly effective in the sterilization of carriers The effectiveness of atebrin as a schizonticide and of plasmoquine as a gametocide was confirmed

MANSON (Assam) reports trials with atebrin and plasmoquine in 106 cases of benign and malignant tertian malaria Atebrin alone was given in 26 cases with four relapses A combination of atebrin (0 1 gm) with plasmoquine (0 0033 or 0 005 gm) was given in 75 cases with only seven relapses, or 9 33 per cent , and it is concluded that this combination is the best form of treatment at present available Toxic symptoms were limited to cases showing excess or deficiency of gastric hydrochloric acid or pathological changes in the gall-bladder No toxic symptoms were noted in normal patients this bears out the relation of gastric *pH* to such symptoms Atebrin-musonat was tried in only five cases with one relapse Manson describes this as a relapse rate of 20 per cent ; this seems hardly fair, but he draws no conclusions from so small a series

HAY, SPAAR, and LUDOVICI (Kandy, Ceylon) have treated over 3500 cases by injection with both atebrin dihydrochloride and atebrin for injection They have had no cases of collapse after injection and no death attributable to the drug For adults the dose employed was 0 15 of the dihydrochloride, repeated in twenty-four hours This was followed by oral treatment of two tablets of 0 1 gm daily for six days, bringing the total to 1 5 gm , which they regard as a safe limit In one case the patient confessed to having swallowed ten tablets the day he received the injection, but he suffered no ill-effects from the big dose With atebrin for injection they recommend a dose of 0 3 gm intramuscularly, followed by oral treatment to a total of 1 5 gm

PETER reports clinical trials with atebrin at the Malaria Research Station, Gurbanesti, Rumania He finds that atebrin has a marked affinity for the parasites, to which it becomes firmly bound , on this account the amount required should be regulated by the number of parasites present rather than by the weight of the patient Metabolism plays a part in its action, and this can vary in the same patient Milk and foodstuffs containing cellulose absorb atebrin and diminish its therapeutic effect

SIMEONS describes mass treatment with atebrin for injection in a village in Ceylon A hospital staff of sixty-five persons received two injections each at an interval of twenty-four hours Parasites and fever were completely controlled in three days and no serious toxic symptoms were observed During an epidemic 240 villagers were treated in the same way with equally good results In a mill area 5650 persons received two injections each It was found that solution more than a few hours old produced giddiness or even fainting in a few persons

BERCOVITZ (Hainan, China) reports on the use of atebrin for injection (atebrin musonat) and concludes that it is safe in injections of 0 3 gm daily for two days No disturbance was seen in pregnant

women Tertian parasites were eliminated from the circulation after two injections The crescents of *P falciparum* are persistently present for many days after injection and seem to be affected only by plasmoquine While atebrin destroys the parasites, the tonic action of quinine is noticeably absent, and it is suggested that the two injections should be followed by quinine and plasmoquine to restore the general tone of the patient VARDY (Singapore) gave injections of atebrin musonat in fifty serious cases, in thirty two of which the malaria was cured within forty eight hours The dosage is 0 6 gm in forty eight hours, then no more For intravenous administration the adult dose of 0 1 gm should not be exceeded, this may be given twice or three times in twenty four hours, injected slowly Intramuscular injection is preferable In the cases recorded, only two of which were treated intravenously, *P vivax* disappeared in two or three days and *P falciparum* in four or five days

Toxic Effects —As already mentioned, the toxicity of atebrin is low, the yellow pigmentation due to the acridine content being the usual symptom Plasmoquine is more liable to produce untoward effects, though with ordinary care these usually may be avoided It appears, however, that combined treatment with atebrin and plasmoquine is more liable to be attended with untoward symptoms than treatment with either drug alone

In a report on the use of atebrin, BANERJEE (Suri, Bengal) refers at some length to the toxic symptoms occasionally produced These include yellow pigmentation (harmless), epigastric pain, headache, incontinence of semen, vertigo, haemoglobinuria (in one case only, following atebrin and plasmoquine) bleeding nocturnal amblyopia, palpitation, and mental symptoms Most of these occurred in only a few cases, the mental symptoms were more frequent but passed off or were easily treated Toxicity is enhanced by combination with plasmoquine, and to a less extent with quinine The toxicity is similar to that of the hyoscine group or to the symptoms produced by encephalitis It is essential that the urine should be tested regularly to determine elimination of the drug

UDALAGAMA (Ceylon) reports seven cases of mental excitement following injections of atebrin musonat in a series of 644 cases The mental derangement was only temporary The symptoms were excitement, giddiness, and the appearance of intoxication, they passed off untreated, or were relieved by simple sedatives Several similar cases were described in this place last year (PRESCRIBER, 1935, Sept, 280)

MENON (Pahang) reports a case of severe malaria in which an epileptiform fit followed two injections of atebrin musonat Intramuscular injection of quinine (15 grains) brought the patient round and he had no further fits Whether the fit was caused by the malarial infection *per se* or was a toxic manifestation of atebrin is not known The malaria was apparently unaffected by atebrin but became rapidly controlled under quinine Menon realizes that in

the circumstances it is unfair to blame the atebrin, but he thinks the case should be recorded.

FERNANDO and WIJERMA (Colombo) report a case of death after injection of atebrin. Two intramuscular injections had been given two months before the patient was admitted, and in view of the yellow pigmentation and the absence of atebrin from the urine the case was diagnosed as atebrin poisoning. The patient was treated with quinine and digitalis, but he gradually sank and died after two days in hospital. It was evidently a case of idiosyncrasy, and it is possible that the patient had been taking atebrin by mouth since the injections, though this is not mentioned. The high concentration of atebrin in the tissues suggests this possibility.

Miscellaneous Remedies.—The success of plasmoquine and atebrin has drawn many workers into the field, and numerous compounds have been put forward in the hope that they may be found of equal efficacy and free from the drawbacks of these drugs. Mention may be made of the work of British chemists on the quinoline and acridine derivatives. Many such derivatives have been prepared, their antimalarial properties are being carefully tested, and the work is still proceeding. Previous work in this direction has been mentioned in recent reviews, and during the past twelve months reports have been published by KERMACK, MUIR, and WIGHT (Edinburgh), by KERMACK and WIGHT, by CLEMO and HOOK (Newcastle-upon-Tyne), and by CLEMO, MCILWAIN, and MORGAN. These reports are mainly technical, but they show that our chemists are fully alive to the necessities of the situation.

Tebetren.—A combination of methylhydrocupreine with an acridine dye and a bile salt has been introduced under the name of *Tebetren*, which is described as methyl-hydrocupreine-methylacridine dehydrocholate. The bile salt is said to render the compound less toxic. It decreases the number of parasites in the peripheral blood, and in this respect appears to be intermediate in action between atebrin and quinine.

Malarcan.—This compound appears to be on the same lines as tebetren: it is described as 'a compound of a stereo-isomeric base of methyl-cupreine with methyl-acridinium chloride and hydrocholic acid.'

Giemsa-C77.—This quinine derivative, prepared experimentally by Giemsa, is a red azo-dye obtained by the condensation of hydrocupreine. Chemically it is 6-methoxyquinoline-8-azo-hydrocupreine. It is said to act like quinine on the parasites of subtertian and quartan malaria but to be somewhat inferior in benign tertian.

Quinacrine.—The composition of this is said to be identical with that of atebrin. Several French workers have reported on its use. It is said to be free from toxic effects and to have a wide margin between the therapeutic and the toxic dose.

Rhodoquine.—A large number of compounds, several of which

have been found to have some action in malaria, have been produced in Fourneau's laboratory. Of these, F710 or rhodoquine, is described as a quinoline derivative closely resembling plasmoquine. Another of these, F915 or rhodoquine-U, is a similar compound combined with acetarsol (stovarsol). Others, named F574 and F852, are very similar to plasmoquine, differing slightly in the character of the side-chain.

Plasmocide.—Russian chemists have produced a compound known as plasmocide or 'antimalarene-B.' Chemically this appears to be identical with rhodoquine, except that it is a salicylate instead of a hydrochloride. It appears to be less toxic than plasmoquine. USPENSKAYA (Moscow) reports successful treatment of thirty-two cases of quartan malaria in the Caucasus by its means. Treatment consisted of four courses of three days: during each course 0·03 gm. was given three or four times daily.

Antimony.—The use of antimony as a stimulant to the reticulo-endothelial system in cases resistant to quinine, plasmoquine, and atebrin is reported by DE NUNNO (Siena). He gave intravenous injections of antimony tartrate, one per cent. solution in distilled water, the dose beginning with 1 c.cm. and being increased gradually to 14 c.cm., given on alternate days. After four or five injections the spleen becomes smaller and by the end of the course it usually becomes normal.

Blackwater Fever.—Discussing the aetiology of blackwater fever, KRISHNAN and PAI (Calcutta) come to the conclusion that this condition is not an independent disease but a manifestation of malaria. In its causation probably a special 'biological strain' of the malarial parasite is concerned. This strain has a distinct biochemical activity. Its peculiar mode of attack on the host probably leads indirectly to the production of haemolysis and haemoglobinuria. This assumption recognizes the prime importance of the host factor not only in inducing this 'biological' variation but also in producing the predisposition to haemolysis. The two most important predisposing factors are a damaged reticulo-endothelial system and a diminution in free cholesterol involving both the red cells and the plasma, the latter determining the extent of haemolysis and the former the degree of haemoglobinuria. The sudden severe intravascular haemolysis is explained by the presence of a haemolysin, which it is suggested is the end result of a damaged liver and alterations in metabolism of carbohydrates and fats. Probably it is an unsaturated fatty acid or a lyso-lecithin.

CHESTERMAN (Belgian Congo) reports a case of blackwater fever occurring in a negro child aged 2½ years. Haemoglobinuria was evidently precipitated by a dose of quinine given during a febrile period to a child whose tolerance had been retarded. While natives from non-malarial regions are suspectible to this disease, those in endemic zones are usually immune. In this case copious drinks of 2·5 per cent. solution of sodium bicarbonate soon brought the urine

to normal, and quinine was subsequently given without untoward result

CHOPRA, SEN, and BHATTACHARYA (Calcutta) state that many cases are encountered in Bengal and Assam every year and most patients give histories of repeated attacks of malaria and of medication with quinine for prolonged periods They describe a case occurring in a girl aged 11 years, the special features being (*a*) increased fragility of the corpuscles, (*b*) reduction in their electric charge, and (*c*) diminution in serum albumin with increase in euglobulin, pseudoglobulin, cholesterol, and calcium Atebrin and plasmoquine did not precipitate the attack, but quinine did on two occasions out of three It is thought that the haemoglobinuria was due to other factors besides quinine

MOSTERT (Pretoria) says that the regular quinine taker rarely if ever suffers from this complication Instead, by keeping the system free of malaria and the blood relatively pure, prophylactic quinine appears to be the best safeguard against blackwater fever In Northern Rhodesia most cases of blackwater fever occur immediately after the rains and are precipitated either by a chill or by a combination of a chill and quinine The principle of treatment is to give an initial purge to get rid of the excess of bile, plenty of fluid to dilute the haemoglobin and help it through the kidneys, and absolute rest to protect the heart After an attack the patient is very weak and anaemic and requires careful feeding and tonics

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to be due to infection, the result of lowered resistance Absence of vitamin A has been said to lead to the production of urinary calculi

Vitamin A has been used clinically with some success in the treatment of puerperal sepsis, measles, and pneumonia, also in neuritis and certain nerve affections It is obtainable commercially as a concentrate in almost pure form, the international unit being the activity of 0 6 microgramme (0 006 mg) of pure β carotene

Vitamin B.—This is now styled the vitamin B complex, it being known to consist of at least six distinct factors Of these B_1 and B_2 (the latter being known also as G) are the most important Both are contained in marmite, or autolysed yeast, yeast being a rich source of the vitamin

Vitamin B_1 —This is the antineuritic factor It has been prepared in almost pure crystalline form and is known as *Antineurin*, its formula being $C_{12}H_{18}ON_4Cl_2S$ It is water soluble and is fairly resistant to heat, though readily destroyed by alkalis It occurs most abundantly in yeast, and is found also in cereal germs, rice-polishings, liver, and peas, and to a less extent in milk, egg yolk, and green vegetables Recent reports from America state that the pinto bean has proved to be a rich source of the vitamin The international unit is the antineuritic potency of 10 mg of the international standard adsorption product Therapeutically it is used in the prevention and treatment of beri-beri it has also been employed with success in the treatment of certain types of neuritis, and in the correction and treatment of anorexia Its absence from the diet (avitaminosis B) appears to be related to disturbances of carbohydrate metabolism

Vitamin B_2 —This factor has been styled vitamin G in America, and has hitherto been regarded as the anti pellagra vitamin Its chemistry is being studied but is not fully understood it is believed to be identical with lactoflavin or ovoflavin The most recent work indicates that it consists of two factors—one, a flavin which promotes growth without affecting skin conditions, and for which the term B_2 is to be retained, and another to which the anti pellagra influence is due, this being styled B_6 Vitamin B_2 is fairly heat-stable Vitamin B_6 is said to be present in fats and concentrates have been prepared for experimental purposes from fish muscle and from the germ of wheat and maize No standard has yet been fixed as its exact nature is not sufficiently understood Therapeutically it is used only as a component factor of vitamin B complex

Other Vitamin B Factors —Of the other vitamin B factors little is known Vitamin B_3 is thermolabile, it occurs in yeast and wheat embryo and prevents loss of weight in pigeons fed on polished rice plus B_1 Vitamin B_4 is also thermolabile but B_5 is more stable A factor called *gamma* (γ) has also been recognized, and a 'casein factor,' which is believed to be necessary for growth, has been detected in some forms of casein, also in milk, lettuce, and liver

Therapeutic Uses of Vitamin B Complex.—For medicinal purposes the vitamin B complex is used, either as marmite or as one of the several preparations on the market purporting to contain this vitamin along with others. Certain forms of anaemia have benefited from the administration of marmite. The therapeutic uses of vitamin B_1 have already been mentioned.

Vitamin C.—This factor has aroused considerable interest during the last few years. It is the essential antiscorbutic factor in orange and lemon juice, and it is believed to have something to do with changes in the dentine of teeth. Absence of this vitamin from the system disturbs the oxidation-reduction process of cell function and gives rise to scurvy; moderate deficiency leads to capillary fragility and to defective dental calcification. Vitamin C occurs in most fresh fruits and vegetables; it is present in considerable quantity in the adrenals, this quantity being greatly decreased under conditions that give rise to scurvy. It is soluble in water, and is fairly stable under ordinary conditions but is easily oxidized in fruit juices. Recent work has established its identity with ascorbic acid (known in America as cevitamic acid), a crystalline substance having the formula $C_6H_8O_6$. Ascorbic acid exists in large quantities in the fruit of Hungarian red pepper (*Capsicum annum*) from which it is easily obtained. Ascorbic acid has also been prepared synthetically. Only the laevo form has antiscorbutic properties; dextro-ascorbic acid is inert. Synthetic *l*-ascorbic acid is obtained commercially in tablets. The international unit for vitamin C is 0·05 mg. of *l*-ascorbic acid. Estimation of the vitamin is made by biological methods.

Therapeutic Uses.—Several reports have been published describing the successful use of ascorbic acid in cases of scurvy. An American worker reports its use in cataract: the results in senile cataract were gratifying, while in the cataract caused by dinitrophenol poisoning its action has been surprisingly rapid, at the same time the neuritis and other toxic symptoms showed diminution. Ascorbic acid inactivates diphtheria toxin and promotes resistance to diphtheria infection. Solutions of ascorbic acid have been found to cause haemolysis when injected intravenously, and it has been suggested that such solutions should be neutralized by the addition of half the amount of sodium bicarbonate, making a solution in normal saline of approximately one per cent. strength. Other uses to which ascorbic acid has been put are capillary fragility, capillary haemorrhage, haemophilia, Addison's disease, scorbutic anaemia, and intestinal tuberculosis. Most of these applications have been described from time to time in the Therapeutic Abstracts which appear in these pages.

Vitamin D.—This is the factor about which most is known. It is the antirachitic factor in cod-liver and halibut-liver oils and has been prepared in pure crystalline form as *Calciferol*. It is present in the official solutions of irradiated ergosterol (liquor ergosterolis

New Drugs and Preparations.

[Under this heading are given brief notices of new non secret products as they appear on the market or are mentioned in medical literature The notes are intended for reference only, and must not be taken to imply anything in the nature of a recommendation In most cases the information is derived wholly or mainly from makers' advertisements]

Ammoket —An elixir of ammonium mandelate containing the equivalent of 3 gm of mandelic acid in each tablespoonful dose For treatment of urinary infections (Boots, Nottingham)

Paractol —A white crystalline powder, soluble in water and consisting of betaine and glutamine hydrochlorides In packets containing one dose of 3 gm (45 grains) equivalent to 37 drops of dilute hydrochloric acid For treatment of gastric conditions in which hypochlorhydria is a feature (Homburg Pharma Ltd , London)

Phospho-Mandelate (Collosol Brand) —Consists of mandelic acid and ammonium phosphate, put up in separate envelopes for the treatment of urinary infections, in boxes sufficient for six days' treatment (see PRESCRIBER, June '36, p 216) (British Colloids Ltd , London)

Pitexan —A standardized preparation of anterior pituitary in capsule form, active when given orally Recommended for use wherever the anterior hormones cannot be given by injection (Paines & Byrne Ltd , Greenford)

Prontosil —The new synthetic compound for the treatment of puerperal and other streptococcal infections mentioned in our issue of January 1936, p 36, is issued by Bayer Products in tablets of 5 grains (0 3 gm) and ampoules of 5 c cm for oral and intramuscular administration respectively

Proseptazine and **Soluseptazine** —Synthetic organic compounds having a specially destructive effect on streptococci Proseptazine is for oral administration (tablets, 0 5 gm), soluseptazine is for subcutaneous intramuscular, or intravenous injection (ampoules 5 p c solution) Both are white, odourless and tasteless substances and are recommended for the treatment of infections caused by haemolytic streptococci These drugs are in the experimental stage but supplies are available for clinical trial (May & Baker, Dagenham)

Scuroform Dental Solution —A solution containing 10 per cent of butyl para aminobenzoate (a local analgesic described in our issue of April p 130) in glycerin and alcohol Applied locally as an analgesic in dental work Phials 1 c cm (May & Baker, Dagenham)

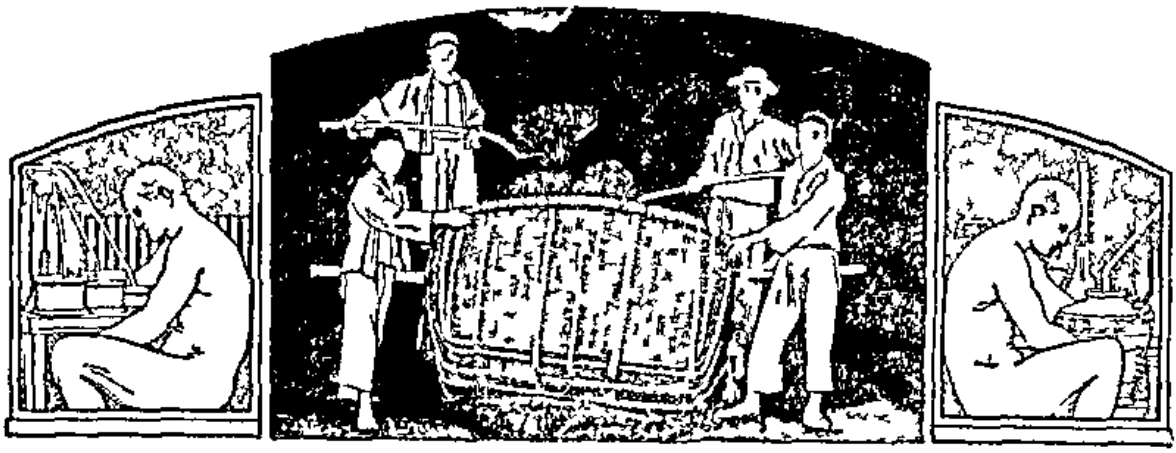
Snake-bite Serum —Messrs Boots announce that supplies of the Pasteur Institute Anti venom Serum are now available at certain of their branches in London, Edinburgh, Oban Bournemouth and Nottingham

Vibex —A standardized solution of vitamin B, for parenteral administration in cases of vitamin B deficiency—progressive polyneuritis alcoholic neuritis and subacute combined degeneration of the cord Prepared from wheat germ and presented in solution free from proteins and lipoids and biologically standardized Ampoules 1 c cm (Parke Davies, London)

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REVIEWS OF BOOKS.

The Anaemias. By Janet M. Vaughan, D.M., Oxon., M.R.C.P.Lond. Second Edition. Pp. 309. (Milford. 12s. 6d.)

The first edition of this work appeared in 1934, and while no spectacular additions to knowledge have been made in the last two years—to quote from the author's preface—much of the previous rapid advance has been consolidated, and considerable revision and additions have been necessary; the present edition is some sixty pages larger than its predecessor. Anaemia being merely a symptom resulting from lesions elsewhere in the body, our author begins by explaining the normal standard values of blood elements and the factors essential to normal erythropoiesis. This leads to a classification of the anaemias in which certain revision has been rendered necessary—for example the author supports the view that hookworm anaemia is due to deficiency of iron rather than to loss of blood. This and other changes have led to some rearrangement in the sections dealing with the groups of anaemias. The book is thus a faithful reflection of the present state of knowledge by a recognized authority and can be confidently recommended for study and reference. T. S.

The Endocrine Organs in Health and Disease, with an Historical Review. By Sir Humphry Davy Rolleston, *G.C.V.O.*, *K.C.B.*, M.D., etc. Pp. 521. (Milford. 36s)

This book is virtually a history of the science of endocrinology from its earliest conceptions to the present day—indeed the subsidiary title of 'historical review' might well receive more prominence. The work is based upon the Fitzpatrick lectures delivered in 1933 and 1934, but it has been amplified, extended, brought to date, and furnished with an elaborate index. When one considers the difficulty in these rapidly moving times of bringing a volume of this size fully to date, one can compliment the author on his success, as even the most recent developments are included down to last year. The author freely acknowledges his indebtedness to current literature, and his lists of references are not the least valuable part of the work. The treatment of the various endocrine organs is systematic and thorough, and as a concise presentation of the science as it stands today as well as a review of its past history the work is without a rival. The book is well illustrated, mainly with portraits of endocrinologists of the past, brief sketches of whose lives embellish the text. T. S.

Origins and Development of Applied Chemistry. By J. R. Partington, *M.B.E.*, D.Sc. Pp. 597. (Longmans, Green. 45s.)

Applied chemistry covers a large field: indeed there are few sciences, arts, or industries today in which chemistry does not take a part. To trace the origins and development of applied chemistry is therefore a huge task, a task which Professor Partington has accomplished with great thoroughness. He tells us in his preface that the original draft of the work was almost double the length of the present text, and the result of his condensation is a model of conciseness. He traces in an

interesting and very readable manner the development of chemistry as shown in the metals, stones, pigments, foods, drugs, and such like of Egypt, Babylonia, Asia Minor, Persia, Phœnicia, Palestine, and other countries About 7000 foot-note references are given and there are no fewer than five indexes including one of Greek words The book contains a mass of information, authoritative, well documented, and readable, and should prove of great value as a work of reference to those engaged in scientific research An added interest is imparted to the book by its medical references whereby the evolution of the healing art may in some measure be traced T S

The Chemistry of Natural Products related to Phenanthrene By L F Fieser, Associate Professor of Chemistry, Harvard University Pp 358 (Chapman & Hall 32s 6d)

This is No 70 of the series of American Chemical Society Monographs, a series which has already done much to assist medical science, and of which this contribution is by no means the least important. The chemistry of phenanthrene, a derivative of diphenyl, is first discussed, and we are then shown its relationship to the morphine group, to cancer-producing hormones, to sterols and bile acids, to the sex hormones, to heart poisons and cardiac glycosides, and to the saponins The matter in places is rather technical in character and of interest mainly to biochemists and others engaged in research work, but it is possible with little difficulty to extract such portions as are of real interest to the physician While each subject is developed separately, special attention has been given to their correlation, and the book provides a comprehensive and thoroughly readable account of the disclosures of recent research T S

Incompatibilities in Prescriptions By E A Ruddiman, Ph M, M D, and A B Nichols, Phar D, B Sc Sixth Edition Pp 337 (Chapman & Hall 13s 6d)

The sixth edition of this American work bears evidence of careful revision The first 109 pages contain an alphabetical list of drugs to each of which is appended a lengthy list of incompatibles, many of the reactions described are of purely scientific interest and are not likely to be encountered in practice The remainder of the book contains some 500 prescriptions with criticisms the criticisms are not appended to the prescriptions but appear together later under corresponding numbers This is designed simply as an exercise for students the prescriptions are not grouped in any special way and reference to the index is necessary to find any particular combination All this shows that the work is for students rather than for practitioners, but as a students' textbook it reflects much credit on the authors, who have evidently devoted much time and labour to its production

A Hundred Years of Medicine By Wyndham E B Lloyd, M R C S, D P H Pp 344 (Duckworth 15s)

This volume, which is one of the 'hundred years series,' consists of three main sections, in which are reviewed the advances of a hundred years, and an epilogue in which are set out certain still unsolved problems

The second part surveys the advances in medical science during the period from 1835 to the present day: it is the lengthiest and perhaps the most interesting. The epilogue is inclined to be unduly gloomy—we hardly agree with the author that a 'traffic chaos' will occur 'when all the streets of thought are choked with facts.' Obsolete 'facts' have a way of disappearing. In the historical portion the material is well marshalled and the 'high spots' are set forth with great skill. When one remembers that among other things the last hundred years have seen the birth of anaesthetics, antiseptics, vaccines, hormones, vitamins, x-rays, and radium, it will be seen that much ground is covered. Synthetic adrenaline, we may mention, is no longer only half as active as the natural product: it now consists entirely of the 'left-handed' variety. The reduction in the price of insulin was not due to commercial competition but to improvement in the process of manufacture: reductions were announced by the rival manufacturers simultaneously from time to time

These and other small points will doubtless be put right in future editions. Meanwhile one can have nothing but praise for the clear and succinct manner in which the subject has been presented throughout the book. T. S.

Pathology of the Nervous System: A Student's Introduction. By J. Henry Biggart, M.D., Pathologist to the Scottish Asylums Board. Pp. 335. (Livingstone, Edinburgh. 15s)

This book by the Director of the Scottish Asylums Laboratory comes at a time when a new work on neuropathology with special reference to mental diseases is required, especially as it is now generally recognized that research in mental hospitals has in the past been severely handicapped by the unfortunate dissociation between clinical investigation and the controlling and stimulating influence of a well directed neurological laboratory. The author defines his attitude towards research very concisely and clearly: 'to envisage what is happening in the nervous tissues'; this is the key-note of the book.

Every aspect of the subject is carefully treated, and nothing omitted which may prove useful to the investigator. There are chapters on the reaction of the nerve cell and of the interstitial cells to disease, on the cerebrospinal fluid, vascular disease, acute and chronic bacterial infections, virus diseases, injuries, errors in development, and tumours. This last chapter is especially welcome owing to the vastly increased importance which the diagnosis and treatment of these growths has assumed in recent years

The chapters on the diseases due to infections and viruses, as well as those classified as intoxications and deficiency diseases, are very welcome owing to their ever increasing importance; and one is glad to see included the phenomena which occur in the brain after head injuries. Finally there is a short chapter on errors in development.

The work can be strongly recommended to psychiatrists and neurologists. The author has treated his subject very broadly; his style is clear and direct, and the illustrations, of which there are 204, have been well chosen, and are beautifully reproduced. The index and bibliography are very good. Professor Murray Drennan contributes a foreword.

D. O.

A third edition of THERAPEUTIC USES OF INFRA-RED RAYS, by W. A. Troup, M D. (Actinic Press, 10s 6d.), has been issued. The author is to be congratulated on the success of a book that is readable, instructive, and convincing. At a time when infra-red radiation is beginning to be recognized as a valuable adjunct to treatment it is useful to have a treatise that explains the technical as well as the practical aspects of the method. Dr Troup's description of cases is valuable in showing the wide variety of conditions to which infra-red radiation is applicable. The present edition is about half as large again as the last, and nearly three times the size of the first edition.

ALCOHOL IN HOSPITAL PRACTICE is the title of a pamphlet by C. C. Weeks (National Temperance League, 33 Bedford Place, London, W.C.1, 9d) In it is shown how the use of alcohol for medicinal purposes is becoming less and less, the figures for the various hospitals showing a decline during the past 35 years In some cases this decline has been very great indeed, one institution showing a drop from 53·1d. per head in 1900 to 3·3d. in 1934, while all statistics show a decidedly downward trend.

A new edition of FOOD VALUES, by the late Margaret McKillop, M.A, revised and brought to date by Elsie C. Mottram, has been issued (Routledge, 3s. 6d) The subject is one of great importance and is developing very rapidly, and the reviser has fully realized this. The practical side of the subject is made the main theme and this excellent little work receives a fresh lease of life in its revised form.

THE NATURE AND TREATMENT OF ASTHMA, HAY FEVER AND MIGRAINE is the title of a volume of papers published by A. G. Auld, M.D. (H. K. Lewis, 12s 6d.) The author's periodical contributions to the journals for over twenty years have been original and stimulating, and it was well worth his while to collect these papers in book form for they embody the gist of peptone and pyrogenic therapy and enable the reader to consult them easily. They are well worthy of consultation and pondering.

The play by Merton Hodge, THE WIND AND THE RAIN, has been rendered into a novel by the uthor (Cassell, 7s 6d) While a dramatized novel not infrequently scores a success, it is questionable whether the same result attends on a novelized drama When one has not only seen but read the play, the mere rendition of its dialogue in narrative form and the translation of the stage directions into the past tense gives a feeling approaching an anticlimax It is true that chapters have been added describing Tritton's life in London, but these are more or less unnecessary, as the real story is confined to his life in Edinburgh as a medical student And we would strongly protest against the suggestion—more evident in the play than in the novel—that it is always raining in the Scottish Capital. The rainfall in Edinburgh is below the average and very much less than in many other places. Wind certainly, but not rain And we doubt if medical undergraduates, or indeed any other decent people in Edinburgh, garnish their talk quite so freely with American slang and with that most objectionable 'sanguinary' adjective Otherwise the story gives an interesting and enjoyable account of student life in the Capital and will be much appreciated, especially by those who have not had the good fortune to see this delightful play.

Messrs May & Baker Ltd, Dagenham, have issued a new and enlarged edition of their MEDICAL SPECIALITIES in the form of a daintily bound book of pocket size. All this firm's well-known products are fully described, and suitable illustrations brighten the text. The booklet is issued free to the medical profession.

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AFTER THIRTY YEARS.

THIS month THE PRESCRIBER completes thirty years of continuous publication, the first number having been published on the first of October 1906. For some reason one's thirtieth birthday does not have quite the same significance as one's twenty-first or one's twenty-fifth—the 'coming of age' and the 'silver jubilee' are occasions for rejoicing, but the thirtieth anniversary is only a birthday and a sign of increasing age at that. Still to ourselves, and we venture to think also to our readers, the occasion is one of interest and deserves at least a passing reference.

Our predominant feeling at this time is one of gratitude to our numerous supporters — subscribers, advertisers, literary colleagues, and printers—for their assistance in enabling us to maintain an unbroken record for three decades. Many of these have been with us since the beginning, and to all we gratefully record our appreciation of their support. The position held by the journal to-day is one of which its founder may well feel proud, and this position could never have been attained without their willing and able co-operation.

Perhaps the most instructive feature of the present occasion is the opportunity it offers to view the progress of thirty years. Without doubt the period has been by far the most progressive in the history of medicine. Some of the most wonderful advances ever recorded have taken place during that time, and a survey of the thirty volumes in which these have been described reveals not only how far medical science has developed, but also which of these

developments have survived and which have succumbed under the influence of further knowledge. It is pleasant to reflect that the failures have been relatively few and unimportant.

As we have said on previous anniversaries—and we make no apology for repeating it—the aim of this journal has throughout been one of service, the interests of our readers having always been our first consideration. In this policy we have been well supported by our colleagues in the work, and to judge from numerous letters of appreciation our aim has been fully recognized by our readers. By reviewing the progress of medical science during thirty years we trust we have been able to do our little bit in helping the medical profession in their struggle to overcome the ravages of disease.

Mapharside in Vincent's Infection.—DUEHR and associates (Univ. of Wisconsin) report on the local use of mapharside (see PRESCRIBER, 1936, Aug., 260) in the treatment of Vincent's infection. It causes no damage to the mucous membrane of the mouth, while the infection when limited to the gums yields with remarkable promptness to topical application of the powder. For extragingival lesions an occasional intravenous injection may be required in addition.

DUEHR, P. A., WEISSMILLER, L. L., MCINTOSH, R. L., COOPER, G. A., and TATUM, A. L. Mapharsen, a new therapeutic agent for Vincent's infection. *J. Amer. Dent. Assoc.*, 1936, Apr., 652-655.

Salicylates in Rheumatic Fever.—MURRAY-LYON (Edinburgh) finds that sodium salicylate given in adequate doses with double the quantity of sodium bicarbonate benefits the rheumatic fever patient greatly, the disease being rapidly brought under control in the vast majority of cases. Relapses are rare when the patient is taking at least 120 grains daily. All cases, except the most trivial, should *receive this dosage for a month after admission to hospital.* The initial dose to be aimed at in an adult should be 200-240 grains daily, and this amount should be kept up until toxic signs develop or until the temperature has been below 99° F. for twenty-four hours. Thereafter a reduction to 180-150 grains might be allowed for ten days, and after that a dose of 120 grains be maintained till the end of the fourth week. It would be well to continue 60 grains daily until the patient is ready to be allowed out of bed, when 30-45 grains of acetylsalicylic acid might be substituted for a time.

MURRAY-LYON, R. M. Salicylates in rheumatic fever. *Edinburgh Med J*, 1936, Feb., 84-98.

RECENT WORK IN DERMATOLOGY

NOTE —In the arrangement of the various diseases dealt with in this review, it has been thought best to adopt a strictly alphabetical sequence, the only exceptions being those grouped under the head of 'Fungus Infections' and 'Pigmentation' Matters dealing with dermatology generally have been put at the beginning under the heading 'General' For the greater convenience of readers, the references are arranged alphabetically at the end of each section —EDITOR

GENERAL.

Aetiology.—That certain dermatoses are caused by filterable viruses has been generally recognized—warts, molluscum contagiosum, herpes zoster, and varicella being typical examples That other conditions are similarly caused is possible, and from the variety of such manifestations it may be said that virus diseases of the skin show little in common In a recent study of the subject, BRAIN (London) has investigated the above mentioned conditions with a view to ascertaining the cause of skin affections whose aetiology remains unsolved His work helps to confirm the close relationship between zoster and varicella With warts and molluscum contagiosum, although these are known to be infectious in man, he was unable to demonstrate the presence of antibodies in the serum of patients with multiple lesions Transmission experiments with material from cases of dermatitis herpetiformis gave negative results except when staphylococci and streptococci were present Sterile bullous fluid *from a case of pemphigus vegetans was inoculated into* animals without result, and no evidence of a hypothetical virus could be obtained in cases of psoriasis and lichen planus

That the psychic factor is contributory in the aetiology of skin diseases is proved by numerous cases on record A rather curious case is reported by CORMIA and SLIGHT (Montreal) The patient, a man aged 29, suffered from an ill defined eruption of long standing on the arms and legs He was of a masochistic type and obtained relief from sexual tension through excoriation, thus producing lesions which resisted all forms of local treatment and on which various diagnoses had been made, including that of tuberculosis of the skin Protection of the limbs was followed by rapid involution of the lesions

The influence of the thyroid gland on skin conditions is emphasized by VON KUP (Sopron, Hungary), who states that many cases of what looks like eczema are accompanied by unmistakable signs of thyrotoxicosis He mentions the case of a girl aged 16 who for nine months had been treated with ointments and lotions but without avail Raised basal metabolic rate and other signs of hyperthyroidism were present, and when these were treated the 'eczema' subsided

Vitamin Deficiency —In this place two years ago (PRESCRIBER, 1934, Oct , 305) reference was made to reports by Loewenthal and others, who described what was styled cutaneous avitaminosis, an affection involving dryness of the skin, with itching, papular eruption, and folliculitis The absence of vitamin A was obviously the cause Since then the condition has received further attention and it is held by some that absence of vitamin reduces the resistance of the skin to infection

Among recent reports may be cited that of GIBLIN (Port Moresby), who states that he has seen among the natives of Papua a skin condition resembling that described by Loewenthal Eye signs of xerophthalmia usually accompanied the skin symptoms Treatment with cod liver oil soon cleared up the eye signs, but it took considerable time to relieve the skin symptoms, though these eventually disappeared under this treatment

FRAZIER and HU (Peiping) have examined over 200 such cases Hyperkeratosis of the hair follicles, they find, frequently occurs in association with xerophthalmia in young adults Observations on cases of dermatosis in which the classic signs of vitamin A deficiency were absent indicate that the skin may show the only clinically detectable manifestations of this disease SWEET and KANG report similar cases also among the Chinese Specific treatment with vitamin A caused the symptoms to disappear

Reviewing the subject generally, MOURIQUAND and GATÍ show that a combination of vitamin deficiencies may exist with a lack of general alimentary equilibrium Administration of thyroid increases the liability to xerodermia and xerophthalmia in A deficiency With B deficiency sunlight is an important precipitating cause of pellagra, while it is an effective anti rachitic in D deficiency The effects of calcium deficiency and parathyroid control also enter, while the factor of insufficiently mixed diet is important All this goes to show that, as already stated, the absence of vitamin probably lowers the skin's resistance and permits of infection from without

Skin Disinfection —According to a report by the Council on Pharmacy and Chemistry of the AMERICAN MEDICAL ASSOCIATION, the terms 'sterile' and 'sterilization' ought not to be used in connexion with the skin Sterilization means complete absence or destruction of all organisms and the term cannot be used in a relative sense It is questionable whether any chemical agent tolerated by the skin will produce sterility The substances generally employed reduce the bacterial flora to such an extent that they may properly be described as disinfecting agents, and the term 'disinfection' is therefore preferable to 'sterilization'

A simple formula for a mercuric chloride solution for skin disinfection is offered by VAICHULIS and ARNOLD as follows Mercuric chloride 1 0 gm , hydrochloric acid 10 c cm , chrysoidin Y 2 0 gm alcohol (95 per cent) 600 c cm , acetone 200 c cm , water to 1 litre This solution has a high phenol coefficient, it penetrates the skin and

removes fat, it does not irritate, and the colour disappears from the skin within twenty-four hours. It gave efficient skin disinfection in *nearly 500 cases.*

HILL (Johns Hopkins Hosp.) finds that under conditions of practice no antiseptic can invariably sterilize heavily infected skin. Aqueous solutions of antiseptics are unsuitable for skin disinfection: surgical solution of mercurochrome (a solution in water, alcohol, and acetone) is more effective than tincture of iodine, and much superior to aqueous solution of mercurochrome.

A substance which has recently been recommended for skin disinfection is isopropyl alcohol, $CH_3 . CH(OH) . CH_3$. It must not be relied on to destroy spore-bearing organisms. Being a solvent for creosote it is used for the removal of that substance from the skin to prevent creosote burns.

The use of gentian violet in the treatment of secondarily infected dermatoses is warmly advocated by FLORANCE (Sydney), who says that he got the idea from seeing it successfully used in the Royal Infirmary, Edinburgh. He recommends an aqueous solution, having found the alcoholic solutions too irritating, and he uses a 2 per cent. solution in the treatment of impetigo, impetiginized eczema, intertrigo, eczematoid ringworm of the feet and hands, and seborrhoeic dermatitis. Gentian violet is of little use in the treatment of deep-seated pustular conditions.

Hyperpyrexia.—As the result of a study of the effect of hyperpyrexia in the treatment of chronic recurrent dermatoses, ROSEN, ROSENFELD, and KRASNOW (New York) report that when induced in mild form by external heat through infra-red rays in a moist cabinet *it effected temporary clinical improvement in seventeen out of* eighteen patients so affected. Of these eleven have shown relapses after varying periods. Some were benefited sufficiently to resume their former occupation.

Ointments and Powders.—According to MULZER (Hamburg), it is a mistake to prescribe ointments in cases of skin disease, especially the eczematous kind, without first ascertaining the nature of the patient's skin. Skins of the seborrhoeic type—the more common—are intolerant of ointments, which cause retention of the secretions and provoke corresponding reactions: in such cases dry treatment such as dusting powder is indicated. The skin suitable for treatment with ointments is of a dry scaly character with dry lustreless hair. When a man prefers powder to ointment after shaving, or when a woman finds it necessary to wash her hair frequently, the skin is of the seborrhoeic type and ointments are contraindicated.

AMERICAN MEDICAL ASSOCIATION. Use of the terms "sterile," "sterilize," and "sterilization" (Report of the Council of Pharmacy and Chemistry) *J.A.M.A.*, 1936, July 4, 38.

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GIBLIN, W F Lowenthal's new cutaneous manifestation in the syndrome of vitamin A deficiency observed in Papuan natives *Med J Australia* 1936, Feb 8 202 203
HILL J H The action of mercurochrome and other drugs on normal human skin and in infected wounds *J A M A* 1935 July 13 100 104
MOURIQUAND G and GATÉ J Avitaminoses en dermatologie *Ann de derm et syph*, 1935 Oct 881 915
MULZER, P Uber die Vorteile der Trockenbehandlung gegenüber der Behandlung mit fetthaltigen Salben bei Hautkrankheiten *Dtsch med Wschr*, 1936 May 15 805 807
ROSEN I ROSENFELD H, and KRASNOW, F Effect of hyperpyrexia in the treatment of chronic recurrent dermatoses clinical and biochemical studies with special reference to lipids and lactic acid, preliminary report. *Arch Derm & Syph* 1936 Mar 518 534
SWEET L K and K'ANG H J A clinical and anatomic study of avitaminosis A among the Chinese *Amer J Dis Child*, 1935, Sept 699-734
VAICHULIS J A and ARNOLD L Compound colored alcoholic solution of mercuric chloride for skin disinfection *Surg Gynec & Obstet* 1935 Sept, 333 335
VON KUP, J Symmetrische allergische Hautveränderungen bei Thyreotoxikose *Dtsch med Wschr*, 1936 Apr 3 538 539

ACNE.

In a general article on the treatment of acne, GRAHAM-LITTLE (London) recognizes two distinct types—pustular and non-pustular For the pustular type he advises the removal of any septic focus such as tonsils or teeth, and the administration of vaccines in large doses with careful attention to the patient's diet and mode of life X-ray therapy should be reserved for obstinate cases ultraviolet radiation is much less dangerous, but it is less effective and its action is capricious, in some cases it aggravates the condition The non pustular type usually disappears spontaneously as the patient matures in years

BELISARIO (Sydney) strongly advocates x-ray therapy With suitable precautions and technique, which he describes in detail, and with the use of suitable and accurate dosage, he claims that the treatment is successful in 95 per cent of cases Scarring is prevented by appropriate after-treatment, while relapses occur only in persons of low general health or near the age of puberty

LAST and STEIN (Vienna) state that short-wave therapy, while it does not effect complete healing, will shorten the duration of certain cases and cause the absorption of infiltrations without producing scar tissue They describe four cases in which improvement was effected

It is held by many that carbohydrate diet should be avoided by patients with acne This question has been investigated by CRAWFORD and SWARTZ (Harvard Univ), who selected ten patients with severe pustular acne, put them in hospital, and fed them for two weeks on a diet rich in carbohydrates with daily intravenous injections of

dextrose. Five showed definite improvement, two slight improvement, and none was worse. Maintenance of this diet resulted in continued improvement, which shows definitely that carbohydrate diet is not inimical to patients with acne.

The occurrence of acne at puberty has suggested that the condition is due to endocrine imbalance involving the sex hormones, a report of the successful use of which appeared in last year's review (PRESCRIBER, 1935, Oct., 302). ROSENTHAL and NEUSTAEDTER (New York) report a series of examinations of the blood of young girls suffering from acne which revealed a general deficiency of the oestrogenic substance, a finding which leads to the conclusion that there is abnormality of formation or of utilization of the sex hormone. Whether this is causal or merely incidental they are unable to say. As an experiment, LAWRENCE and FEIGENBAUM (Boston) treated fifteen acne patients with antuitrin-S with good results. In a later paper, LAWRENCE describes a further series of cases in which the response was very satisfactory: the acne cleared up, and where genital hypoplasia existed this became normal at the same time. It is probable that the imbalance involves the anterior pituitary gonadal mechanism.

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LAWRENCE, C. H, and FEIGENBAUM, J The treatment of acne vulgaris with pregnancy urine extract *New England J Med*, 1935, June 27, 1213-1214
ROSENTHAL, T, and NEUSTAEDTER, T. Estrogenic substance in the blood of patients with acne *Arch Derm & Syph*, 1935, Oct, 560-562

ANTHRAX.

GOLD (Chester, Pa.) reports a study of ten cases of anthrax in a mill which handled goat hair imported from the East. The diagnosis was confirmed by culture from the lesions, and the bacilli were recovered by culture from the goat hair. Human anti-anthrax serum was used in treatment of all the cases. In one case injection was made locally with the result that the oedema spread along the tissue spaces: this case proved fatal. All the others recovered on treatment with intravenous or intramuscular injections of serum in doses ranging from 300 to 1350 c cm. ROBERTSON (Boston, Lincs) reports a case of anthrax in a farm labourer who had been working with manure containing residue from wool factories. Prompt administration of anti-anthrax serum effected rapid and complete recovery.

GILBERT (N. Rhodesia) reports nine cases of pustular anthrax occurring among the natives of Barotseland, in which injections of

neoarsphenamine were used with success One intravenous injection of 0 6 gm was usually sufficient In cases where the oedema persisted after twenty-four hours a second injection was given Seven of the patients made remarkable recoveries, two (aged one year and five years) died—of these one was moribund on admission and the other developed fatal ascites Gilbert suggests that if arsphenamine is given within four days of the appearance of the pustule recovery is almost certain

Dorling (Tientsin) remarks that in China pustular anthrax is frequent and is usually acquired by infection from the skins of animals He has found the disease very amenable to local injections of phenol, 5 per cent in water, 2 or 3 c cm being an average dose for a malignant pustule The injection is made through two, three, or four punctures around and into the base of the pustule and a simple dressing is applied Often one such injection is sufficient, usually two are necessary If any part of the pustule shows signs of progressing a further injection is made at this point The oedema and the general symptoms disappear with remarkable rapidity For the great majority of cases this is all the treatment required

Dorling G C Anthrax with special reference to the treatment of malignant pustule by local carbol c injections *Chinese Med J* 1935 July 662 666
Gilbert F W Human anthrax in Barotseland treated with novarsenobenzene *Lancet* 1935 Dec 7 1283 1285
Gold H Studies on anthrax clinical report of ten human cases *J Lab & Clin Med* 1935 Nov 134 152
Robertso t D C Anthrax in a farm labourer *B M J* 1936 Apr 4 695

BURNS.

Tannic Acid —Taylor (Indianapolis) calls attention to what he describes as the misuse of tannic acid in the treatment of burns This treatment was originally advocated for use in severe cases only, but it is now frequently employed in milder 'second degree' burns The action of tannic acid applied to a burned area in which viable islands of the germinal epithelial cells still survive is not limited to the dead tissue Many of the epithelial cells that might take part in the repair of the denuded area are also tanned, and repair is thus delayed Coagulation treatment of burns should be reserved for the more severe types, for the majority of second degree burns bland wet dressings and ointments are best

Reference was made last year (Prescriber, 1935, Oct, 304) to an improvement on the tannic acid method, in which the usual spray of 5 per cent tannic acid solution is followed by the application of a 10 per cent solution of silver nitrate This method has since been tried in fourteen cases by Cotter and Kimbel (Christchurch, N.Z), who report that by this means shock is reduced to a minimum, the patient is more comfortable, nursing is facilitated, absorption of toxic products is very slight, epithelization is rapid, and scarring is much lessened On the application of silver nitrate a firm black coagulum immediately forms and dries within a few minutes This

coagulum is thinner and more flexible than with tannic acid alone; there is no danger of argyria, and the application causes no pain.

Mercurochrome.—TURNER (Anglo-Iranian Oil Co.) reports most encouraging results from the use of mercurochrome. Tannic acid produces a coagulum that is coarse, tough, and opaque; it is 'dirty' and destructive to bed-linen, and the solution is unstable. Mercurochrome, on the other hand, forms a thin transparent crust; it does not precipitate protein, injure bed-linen, or irritate the tissues, and its solution is stable. After the usual preparation of the burnt area, a 2 per cent. aqueous solution of mercurochrome is applied, and the surface is dried by means of an electric drier. Fresh applications are made on subsequent days.

Acute Toxaemia.—WILSON, ROWLEY, and GRAY (Edinburgh) report three cases in which adrenal cortex extract proved of great value in the treatment of the very dangerous early stage of an extensive burn. In these cases acute toxaemia had developed in a very severe form, and in each case injection of adrenal cortex extract (eucortone) effected recovery when death seemed imminent. The dose was 1 c.cm. for a child and 2 c.cm. or more for an adult injected subcutaneously every two hours. The extract appears to act by increasing the efficiency of the circulatory mechanism: there was no evidence of functional insufficiency of the adrenals.

Iodine Burns.—SUTTON (Kansas City) calls attention to the value of sodium thiosulphate as a remedy for burns caused by iodine. Some skins are very sensitive to iodine, and when this is so a solution of sodium thiosulphate (1 : 200) applied as a compress will at once remove the iodine by combining with it chemically and thus allow the irritation to subside.

COTTER, A. P., and KIMBELL, N. K. B. The tannic acid-silver treatment of burns. *New Zealand Med. J.*, 1935, Dec., 384-388.
SUTTON, R. L. Treatment of iodine burns with sodium thiosulfate solution. *Arch. Derm. & Syph.*, 1936, June, 1062.
TAYLOR, F. The misuse of tannic acid. *J.A.M.A.*, 1936, Apr. 4, 1144-1146.
TURNER, A. C. A contribution to the treatment of burns. *B.M.J.*, 1935, Nov. 23, 995-996.
WILSON, W. C., ROWLEY, G. D., and GRAY, N. A. Acute toxaemia of burns: extract of suprarenal cortex in treatment. *Lancet*, 1936, June 20, 1400-1402.

CALCINOSIS.

This condition has attracted some attention recently. It is characterized by the presence in the skin and subcutaneous tissues of nodules or ridges containing calcium salts, usually phosphate and carbonate. These contain a creamy mass, which eventually discharges, the nodules disappearing and fresh lesions forming. Two forms of calcinosis are recognized—local (*c. circumscripta*), which refers to calcification in lesions already present, and general (c. universalis), which implies an excessive amount of calcium in the blood, due either to destruction of bone (metastatic) or to some

disturbance of the calcium metabolism (metabolic) Prognosis is bad in the metastatic cases, but in other cases it is generally good

COSTELLO (New York) describes a typical case of the metabolic form of calcinosis universalis, which he observed and treated for six years The patient had also multiple hereditary telangiectasis with recurring haemorrhage The unusual feature of the case was that the blood calcium was high when first observed but became normal later with leucopenia

Referring to Bolam's case (see PRESCRIBER, 1935, Oct, 305) in which calcinosis universalis had persisted for over two years without improvement in a child aged 6, WEBER (London) states that in some children the condition definitely improves He cites three cases of his own (girls) to prove this, and remarks that this disease is possibly more common in females than in males

COSTELLO M J Cutaneous calcinosis *New York St J Med*, 1935 Dec 15 1266 1271
WEBER F P Improvement occurring in cases of calcinosis universal s in children *British J Derm & Syph* 1935 Oct 400 404.

DERMATITIS

The subject of streptococcal dermatitis is discussed by KINNEAR (Dundee), who describes it as a superficial inflammation of the skin, characterized in its most active phase by redness, thickening, and an abundant exudation of serum, and as the activity diminishes, by the formation of fine lamellar scales It affects chiefly the folds of the body, especially those behind the ears, and the scalp, but it may be more or less generalized, in which case the folds are still the most affected parts It occurs most frequently in young persons under 20, its duration is indefinite but it is amenable to treatment This consists in daily application of iodine (one per cent) in carbon tetrachloride, with starch poultices to remove matted debris as necessary, and frequently a calamine lotion to soothe the inflammation Ointments are not advisable Coal tar is invaluable in the less active stage

Drug Eruptions —A number of cases have been reported of dermatitis caused by drugs of these the following are the more striking —

Gold —A case of severe dermatitis with hyperkeratosis is reported by ROXBURGH, PAGE, and GORDON (London) The patient, a woman aged 58, was under treatment for arthritis and had received twelve injections of an organic gold salt when an erythema developed with severe swelling and weeping of the skin Later a hyperkeratotic warty condition developed over most of the body and limbs, and gold was found in the scrapings from the warty lesions Injections of sodium thiosulphate and ascorbic acid had no effect The condition yielded to x ray treatment and local applications

Dinitrophenol —Toxic reactions to dinitrophenol have frequently

been reported, including a number of fatalities, but so far exfoliative dermatitis has not been mentioned HITCH and SCHWARTZ (Cleveland, Ohio) report a case of severe dermatitis exfoliativa, along with polyneuritis and cataract, following the ingestion during fourteen days of 28 grains of dinitrophenol in the form of a proprietary slimming remedy

Phenolphthalein—KNOWLES, DECKER, and KANDLE (Camden, N J) describe a case of dermatitis following doses of half a grain of phenolphthalein Experiments with skin grafts indicated that the fundamental process involved was nervous or vascular A rather unusual eruption following the use of this drug is reported by WEISS and KILE (St Louis) A dose of 3 grains caused an acute erythema with a generalized darkening of the skin, the pigment forming in the basal layer of the epidermis Continued ingestion of the drug resulted in a universal bluish black pigmentation which lasted for two years, although by that time it showed signs of fading (*See also* Pigmentation)

Procaine—ROBINSON (Los Angeles) reports a localized eruption following injection of procaine hydrochloride for a minor operation The dermatitis subsided in five days after application of local soothing remedies

Quinine—SETTLE (Waupun, Wis) reports a case in which severe eruption of the hands developed after ingestion of two tablets of a proprietary remedy containing quinine Suitable local treatment relieved the symptoms, which reappeared more than once later on ingestion of the same or similar tablets

Contact Dermatitis—As usual a very large number of reports of contact dermatitis have been published The following are a few of the more interesting cases —

Petrol—In a case reported by BIEDERMAN (Cincinnati) a man showed himself sensitive to the vapour of petrol He had been in the habit of cleaning his hands with petrol, which produced a dermatitis not only on the hands but also on the feet The skin of the forearm was found to be sensitive to the vapour of various brands of petrol, notably the 'ethyl' variety, and it was found that after a few exposures other parts of the body, not directly exposed to the vapour, also developed a rash

Tulip Fingers—In last year's review reference was made to a report by BERTWISTLE regarding the condition known as 'tulip fingers,' an affection which is causing great suffering in the English bulb fields Symptoms begin twelve hours after handling the bulbs and are characterized by intolerable tingling of the finger tip beneath the nail, which becomes exquisitely tender, later the nail separates from its bed The only remedy is to stop handling the bulbs In a later report BERTWISTLE discusses the aetiology of this complaint The testa of the bulb is covered with numerous minute but rigid barbs, which penetrate the finger tips especially beneath

the nail The acidity of the bulb (*p*H 4 2, due to phosphoric and oxalic acids) is not responsible, but it has been found that acetic acid develops as a result of fermentation of the maltose of the bulb, and this is capable of producing intense irritation At one time it was thought that the irritation might be due to bacteria as antiseptics were found to act as a preventive, but it is now believed that these act by preventing fermentation of the maltose Constant treatment of the finger tips with a suitable antiseptic effectively prevents the occurrence of tulip fingers Further work by CAULFIELD (Toronto) shows that the ether soluble portion of the bulb is the cause of the dermatitis Patch tests with ether extracted bulb material cause severe dermatitis, which it was found could be prevented by intramuscular injections of the ether-soluble fraction in mazola oil

BERTWISTLE A. P Tulip fingers *B.M.J* 1935 Aug 10 255 ——Aetiology of tulip fingers (corresp) *B M J* 1936 May 30 1133 1134
BIEDERMAN J B A case of contact dermatitis produced at a distance by the sensitizing agent *J.A.M.A* 1936 June 27 2236 2237
CAULFIELD A H W Tulip fingers ragweed dermatitis *Canad. Med Assoc J* 1936 May 506 510
HITCH J M and SCHWARTZ W P Late toxic results including dermatitis exfoliativa from sulphur (dinitrophenol) *J.A.M.A* 1936 June 20 2130 2132
KINNEAR J Streptococcal dermatitis *Brit J Derm & Syph* 1936, Apr 173 181
KNOWLES P C DECKER H B and KANDLE R P Phenolphthalein dermatitis an experimental study including reproduction of the eruption in skin transplants *Arch Derm & Syph* 1936 Feb 227 237
ROBINSON S S An unusual cutaneous reaction to procaine hydrochloride *Arch Derm & Syph* 1935 Dec. 922
ROXBURGH A C IAGE A P M and GORDON D A case of gold dermatitis with hyperkeratosis *Brit J Derm & Syph* 1936 Mar 137 142
SETTLE R O Dermatitis medicamentosa due to quinine *J.A.M.A* 1936 May 23 1801 1802
WEISS R S and KILE R L. Unusual phenolphthalein eruption report of a case. *Arch Derm & Syph* 1935 Dec 915 921

ECZEMA.

Authorities continue to discuss the nature and aetiology of eczema and to offer definitions of the disease The great difficulty seems to lie in the establishment of a borderline between eczema and dermatitis ROXBURGH (London) offers an aphorism—hardly a definition—which though decidedly unscientific contains an element of truth 'An inflammation of the skin is dermatitis if you know what causes it and eczema if you do not'

ADAMSON (London) states that in all cases which he calls 'eczema' it will be found that the disease started at one particular area as the result of the application of some local irritant It may afterwards be limited to the original site or it may subsequently appear in distant parts, the skin having become everywhere supersensitive to external irritants as a sequel to the primary eczematization He refuses to accept the general opinion that internal factors play any part in its causation, and he reserves the term 'eczema' for a condition that differs from both dermatitis traumatica and dermatitis

venenata These one might naturally expect to result from local irritation, whereas the eruption of eczema is something unique and unexpected

INGRAM (Leeds), on the other hand, is unable to limit his conception of eczema to the entity described by Adamson, though he agrees in describing his affection as an eczema He regards as one and the same thing what is described by some as eczema and by others as dermatitis, excluding only dermatitis produced by gross irritants, such as would inflame any and every skin The common denominator of all these conditions is that the reaction emanates essentially from the capillary loops of the papillae He recognizes an internal factor, an external or provocative factor, and the factor of autosensitization Aetiology is threefold—a background of sensitiveness, an external provocation, and a degree of autosensitization once the eruption is in being

MACLEOD and MUENDE (London) offer a contribution to the discussion based upon a study of the histology of the initial lesion When the antigen or external irritant acts on the skin locally it sets up the eczematous reaction, which consists of the following stages (1) Epidermal release of a diffusible, non specific substance (x substance), which (2) circulates causing fresh patches if excessive or sensitizing the skin if slight (3) This substance irritates the nerve endings and stimulates the basal cells with proliferation of the epidermis, and (4) it has a chemotactic action on the underlying capillaries causing dilatation, exudation of serum, and inflammatory infiltration When the antigen (irritant or foreign body) reaches the skin by way of the blood stream, it acts on the epidermis from beneath, causing itching and proliferation, as seen in gouty eczema or in drug eruptions

HOFFMAN and RATTNER (Chicago) report two cases of acute infantile eczema caused by feeding with cod liver oil In the first case the oil was not suspected until the trouble became chronic, when the oil was withheld and the condition cleared up In the second case the oil was at once stopped and the eczema ceased

Treatment.—In the treatment of eczema the reports all follow the recognized lines and nothing strikingly new has been offered Reference was made a year ago (PRESCRIBER, 1935, Oct , 311) to the work of Cornbleet (Chicago), who had obtained gratifying results from the internal use of maize oil, the action of which he attributed to its high content of unsaturated fatty acids Other workers have used linseed oil for the same reason Following up these reports TAUB and ZAKON (Chicago) tried purified linseed oil in eight cases, but none showed any improvement whatever and they conclude that the treatment is valueless

A correspondent in a pharmacy journal mentions a severe case of eczema which, after trial of all known remedies, yielded in three weeks to pancreatin, one 5 grain tablet thrice daily It is suggested that the patient was not digesting protein to the stage of the amino-acids, the digestion not going beyond the polypeptides These are

known to be toxic, and it would appear that in this particular case the patient was being literally poisoned

ADAMSON H G Eczema its definition and its aetiology *Brit J Derm & Syph*, 1935 Dec, 497 501
HOFFMAN S J, and RATTNER H Infantile eczema from cod liver oil report of two cases *J A M A*, 1936 Aug 15 494
INGRAM J T Definition and aetiology of eczema *Brit J Derm & Syph*, 1935 Dec 502 511
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ROXBURGH A C Eczema and its treatment *Practitioner*, 1936 May, 569-578
TAUB, S J and ZAKON S J The use of unsaturated fatty acids in the treatment of eczema (atopic dermatitis neurodermatitis) *J A M A*, 1935, Nov 23 1675

ERYSIPELAS.

As the result of a study of the incidence of erysipelas, RIDDELL (Stirling) says that the disease does not show any epidemiological features closely allied to scarlet fever The maximum incidence is from October to January and the majority of sufferers are between the ages of 45 and 54, though there is increased incidence in the first year of life Male infants are more susceptible, but in after life the preponderance is with females Poverty and overcrowding cannot be regarded as vital factors

Treatment.—BRAZIL (Coventry) reports a case in which the intramuscular injection of 20 c cm of anti scarlatinal serum gave remarkable results temperature and pulse fell, and pain, oedema, and redness disappeared Five days later a relapse occurred, when a further injection of 27 c cm gave an equally good result In two days the patient was convalescent

KNAPP (Minneapolis) reports treatment of 340 cases with ultra-violet radiation alone A double erythema dose was given, with the lamp about 8 inches from the patient The majority of the patients remarked on the grateful feeling of relief experienced At first oedema increased, but this subsided in 24-48 hours, when the temperature dropped to normal and the area subsequently desquamated In most cases only one sitting was required

The new synthetic remedy *Prontosil*, which has a special selective action on streptococci, has been tried as a remedy for erysipelas by several workers Prontosil is a dark red azo-dye and is available in tablets of 5 grains for oral administration and ampoules of 5 c cm for intramuscular injection GMELIN (Essen) gave it both by mouth and by injection in infants and young children with rapid improvement The skin was coloured orange-yellow and the urine yellowish-red, but these effects were only temporary SCHIRUS (Dusseldorf) found that after administration of 2-6 gm by mouth the disease ceases to spread and the condition rapidly clears up KRAMER (Stettin) gave prontosil parenterally in doses of 20 c cm daily in twenty-three cases with the result that the febrile period was reduced to an average of 4 days as compared with 11 days under other treatment

BRAZIL, W H Anti scarlatinal serum in erysipelas *B.M.J.*, 1935 Nov 2, 840
GMELIN, L Zur Chemotherapie des Erysipels im Kindesalter *Münch med Wschr*, 1935 Feb 7 221-222
KNAPP, M E Treatment of erysipelas with ultraviolet radiation *Arch Phys Therap* 1935, Dec, 711 715
KRAMER, W Ueber Erfahrungen bei der Erysipelbehandlung mit Prontosil *Münch med Wschr*, 1936 Apr 10 608-610
RIDDELL, J The incidence of erysipelas *B.M.J.*, 1935, Nov 16 946 947
SCHREUS, H T Chemotherapie des Erysipels und anderer Infectionen mit Prontosil *Dtsch med Wschr*, 1935 Feb 15, 255-256

ERYTHROEDEMA.

This condition, called also 'pink disease' and acrodynia, was first reported in 1914 by Swift, of Adelaide, Australia Though comparatively rare in this country it is prevalent in Australia and was the subject of a discussion at the B M.A meeting in Melbourne last year It occurs in young children and is characterized by a rash, variable in character from pink to dark red, sometimes like 'prickly heat,' with itching The hands and feet are red and swollen Stomatitis with gingivitis and loss of teeth may occur

WOOD and WOOD (Melbourne), in a general résumé of the subject, discuss its aetiology, which is not well understood Vitamin deficiency, sensitiveness to light, and infection have all been suggested, but none has been proved No specific method of treatment has as yet been established, but much benefit is obtained by attention to the details of symptomatic treatment The great danger lies in cross infection (bronchopneumonia and gastro-enteritis), which may happen if the children are admitted to a public hospital

SWEET (Melbourne) does not agree that there is no specific treatment, holding that all cases, mild or severe, may be cured in a few weeks by ultraviolet radiation The patient is first thoroughly warmed by means of a radiant heat lamp or an electric radiator and is then exposed to radiation from a mercury-vapour lamp. Ten exposures are recommended, given twice weekly, beginning at a distance of 100 cm (40 inches) for two minutes, and gradually reducing the distance and increasing the time to 60 cm (24 inches) for ten minutes Very little other treatment is required

SWEET, G B The treatment of pink disease *Med J Australia*, 1936 Mar 28, 430-434
WOOD, A J, and WOOD, I Pink disease *B.M.J.*, 1935, Sept 21, 527 531

FUNGUS INFECTIONS.

The influence of hydrogen ion concentration on the growth of yeast-like organisms has been studied by HESSELTINE and NOONAN (Chicago), who were led to make the investigation through the difficulty in applying fungicides effectively to the vaginal mucosa They find that mycotic organisms grow best at *p*H 5 5, but substantial growth can take place over a wide range and even in an alkaline medium HESSELTINE and HOPKINS, in a study of fungicides, conclude that the existence of a universal fungicide for clinical purposes

is extremely doubtful, each genus or species requiring a special chemical for its destruction.

The treatment of mycotic infections by means of autogenous fungus extracts is described by ROBINSON and GRAUER (Pittsburgh). These workers were able to prepare cultures from the scales of certain vesicular eruptions and to use these therapeutically with success in a number of cases. They recommend the use of an autogenous 'vaccine' in cases of refractory dermatomycosis. When such is not practicable the use of a stock extract from several organisms is advised. In all cases the intradermal injection should be adjusted to the reaction of the patient.

Some years ago (PRESCRIBER, 1930, Oct., 327) an account was given of the inhalation treatment advocated by Swartz, of Boston. In order to saturate the system with iodine, and thus attack the fungi by way of the blood-stream, ethyl iodide (C_2H_5I) was given by inhalation from a special apparatus in doses of one c.cm., inhalation being spread over twenty minutes. In a recent paper, SWARTZ describes further experience with this method and claims to have effected recovery or improvement in over 230 cases, including epidermophytosis, psoriasis, tinea capitis, and favus. The most common complication was a papulo-pustular eruption, which made its appearance on the diseased area but disappeared soon after cessation of the inhalations. In three cases peripheral neuritis occurred: this cleared up about three weeks after discontinuance of treatment.

Diagnosis.—SWARTZ and CONANT (Boston) advocate direct microscopic examination of the skin to determine the presence of fungi. The treatment of scrapings from the skin with potassium hydroxide, followed by washing and staining in lactophenol and cotton blue, makes possible the easy determination of the presence of fungi. This method of preparing microscopic specimens for examination is effective in that the fungi are definitely stained while the various confusing artefacts are eliminated from the picture. The formula for lactophenol is: lactic acid 1 c cm., phenol crystals 1 gm., glycerin 2 c.cm., distilled water 1 c cm. To this is added 0·5 per cent. cotton blue (C4B Poirrier).

Trichophytin Test.—The genus *Trichophyton* is the causative agent in some forms of ringworm of the scalp and in certain lesions of the hands, feet, and nails. Various species are responsible, but all produce the same allergic reaction when injected intradermally, and this is the basis of the 'trichophytin test.' An extract of several species of *Trichophyton* is used pure or in dilution, and of this 0·1 c.cm. is injected into the forearm. A positive reaction, indicating trichophyton infection, consists in the appearance at the site of injection after twenty-four hours of an area of redness with infiltration, on the surface of which vesicles may appear.

This test has been the subject of controversy and many workers consider that its specificity is open to doubt. KNIERER (Münster,

Westphalia) has compared the reactions produced in thirteen patients with mycoses of the skin with 102 controls including healthy persons and those with non-mycotic affections. He concludes that by itself the test is not sufficiently specific to be of definite diagnostic value but that it might be of use in conjunction with other diagnostic methods.

ROOKX (Liége) says that this test gives a clear reaction in all mycotic infections, which is most marked in trichophytin infection. Intradermal injections of milk also give a reaction in mycotic infections, but this is much less pronounced than in non-mycotic or allergic conditions. To determine therefore whether a skin affection is mycotic or non-mycotic, parallel injections of trichophytin and of milk should be given at the same time.

Actinomycosis.—LORD and TRAVETT (Boston) have isolated from the normal mouth aerobic-anaerobic organisms apparently identical with the actinomyces of the Wolff-Israel type, though they failed to produce lesions when inoculated into animals. It is thought likely that these organisms become pathogenic when injury by a foreign body allows of their entry into the tissues. The mouth appears to be the port of entry, as the most common site of the disease is in the region of the head and neck.

An unusual case of actinomycosis of the hand is reported by HOLLINGSWORTH (Clinton, Mo.). The patient's hand had been pierced by a thorn, after which the part began to swell. The sore was cauterized, but it continued to spread until it covered the entire back of the hand and appeared to be malignant. The entire lesion was excised and dressings of iodine and of copper sulphate were applied alternately and sodium iodide given internally. The lesion healed almost completely. Actinomyces were isolated and identified.

Granuloma.—JORDON and WEIDMAN (Philadelphia) adduce evidence to show that while *Coccidioides immitis* is firmly established as the cause of most, if not all, cases of coccidioidal granuloma in North America, a radically different fungus, *Paracoccidioides brasiliensis*, is the cause of numerous cases in Brazil of a disease which hitherto has been regarded as coccidioidal granuloma.

SOX and DICKSON (San Francisco) report experiments made with a view to finding a suitable remedy for this disease. Eleven drugs and a vaccine were tried on experimental animals, and the only substance giving any definitely favourable result was thymol. This drug is tolerated by human beings in doses up to 6 gm. (90 grains) daily, and it is suggested that thymol should receive a trial in clinical practice.

AYRES, ANDERSON, and TAYLOR (Los Angeles) report the successful use of maggot therapy in a case of ulcerating granuloma of a year's duration. The diagnosis of the lesion was doubtful: a fungus was found in only one of many cultures, and microscopic examination of smears was consistently negative. Under maggot therapy the lesion healed completely.

Hand and Foot Infections —Fungus infection of the feet has become very common, especially in America, where the affection is known as 'athletes' feet' The organisms responsible are *Trichophyton* and *Epidermophyton*, the former being most common in America, in Europe the fungus most frequently found has been *Epidermophyton* The affection is common in those whose feet show a tendency to excessive perspiration In some cases the hands also are affected, possibly by contact

BELISARIO (Sydney) remarks that mycotic infections of the hands and feet are frequently encountered in Sydney, several clinical varieties being recognized The affection is most common in summer, warmth having an aggravating effect, and it is more common in men than in women An alkaline tendency in the sweat predisposes to mycotic infection this may be countered with boric acid, but its effect is too transient—lemon juice is better For routine treatment the parts are bathed night and morning with a pint of hot water to which one drachm of strong solution of lead subacetate is added An ointment of ammoniated mercury (one per cent in lanolin) is thereafter applied In the later stages weak tar or ichthyol applications may be employed, supplemented if necessary by x-rays

THOMSON (London) emphasizes the necessity for precautionary measures the patient should not walk barefoot about the house, and should wear a simple sterilizable foot-covering for the protection of bath mats, etc Separate towels should be used and socks should be sterilized by ironing with a very hot iron Local applications must not only be capable of destroying mycelium but must also be strong enough to penetrate the horny layer, they should be applied conscientiously twice a day and their use must be continued for at least a month after apparent recovery

WISE and WOLF (New York) remark that the majority of vesicular eruptions on the hands of adults are accompanied by fungus infections of the feet, but the eruptions on the hands may not be due to fungi To differentiate between these eruptions a careful history must be obtained from the patient, and a diagnosis of fungus infection should not be entertained without strongly corroborative evidence, the most important being microscopic or other demonstration of the fungus Positive trichophytin reactions are of little significance in such cases

Ringworm of the Scalp.—DEY and MAPLESTONE (Calcutta) report an investigation of fifty-three consecutive cases of ringworm of the scalp seen at the School of Tropical Medicine Of these twenty were referable to *Trichophyton violaceum* (Bodin), and the remainder (with the exception of two cases of favus) were caused by *Microsporon audouini* The cases of *T violaceum* included Europeans, Mohammedans, and Marwaris, and all the patients were under twelve years of age. Nine cases showed secondary infection of the body—in one case it spread over the whole body The existence of *T. violaceum* is recorded for the first time in India it was the only

species of *Trichophyton* found among these cases Dey and Maplestone give reasons for thinking that this fungus would more correctly be classed in the genus *Achorion*

AYRES S ANDERSON N P and TAYLOR G M Maggot therapy in dermatologic practice report of a case of chronic ulcerating granuloma of undetermined etiology in which maggot therapy was used *Arch Derm & Syph* 1936 Jan 21 30

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LORD F T and TREVETT L D Pathogenesis of actinomycosis recovery of actinomyces like organisms from the normal mouth *J Infectious Dis* 1936 Jan Feb 115 120

ROBINSON G H and GRAUER R. C Use of autogenous fungus extracts in the treatment of mycotic infect ons *Arch Derm & Syph* 1935 Nov 787 794

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WISE F and WOLF J Dermatophytosis and dermatophyt ds with particular reference to the differential diagnosis of dyshidrosiform eruptions of the hands and feet *Arch Derm & Syph* 1936 July 1 14

FURUNCULOSIS

FRASER (Royal Navy) reports treatment of a small series of boils and carbuncles on board H M S *Hood* by the occlusive method The dressing used was zinc oxide elastic adhesive bandage (elastoplast) applied directly to the shaven skin and extending well beyond the outer limit of the inflamed area The surrounding skin was sterilized with 1 1000 acriflavine, but no preliminary surgery was attempted *Results were most satisfactory* Men were released for duty at once, and almost immediate relief of pain was afforded Twenty cases were treated, the average number of dressings being two to three and the average number of days under treatment eleven to twelve Only one case received hospital treatment

WHITBY (London) reports on treatment with staphylococcal toxoid Injected intramuscularly this is a safe antigen giving rise

to few minor reactions. It gave a good clinical result in a high proportion of cases of recurrent and resistant furunculosis, and proved useful in the treatment of styes and carbuncles. It was not effective in pustular acne or in sycosis. It is ineffective for skin lesions where the skin itself is peculiarly susceptible to infection. The optimum dose is an individual factor: those in whom the toxoid produces an exacerbation should receive small doses.

FERGUSON SMITH also reports on the use of toxoid in a series of cases of boils. He sums up his experience by saying that toxoid is a more potent and reliable means of raising the antibody-content of the blood than are vaccines, but its therapeutic effects, like those of vaccines, are at best doubtful. If all cases of recurrent boils are treated with either, most will recover, but a critical survey will expose the fallacy of this conclusion. While the figures adduced were not large enough to be conclusive, the trend of his investigation was to emphasize the importance of local factors, and the relative unimportance of the immune state of the patient, in dealing with furunculosis.

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WHITBY, L. E. H. The treatment of staphylococcal skin lesions with toxoid. *Lancet*, 1936, June 27, 1454-1456.

IMPETIGO.

For small infants, FRAZIER (Peiping) recommends ointment of ammoniated mercury. It is non-irritating, non-toxic, and an effective bactericide. For older children he advises painting the lesions with silver nitrate. After softening the crusts with liquid paraffin, they can be taken off easily with forceps. A 5 to 10 per cent. aqueous solution of silver nitrate is applied to the entire surface of the lesion and allowed to dry. No dressing is needed. The coagulating action of the silver nitrate seals the surface of the lesion with a firmly adherent, smooth, black crust. This should not be disturbed. As a rule a single treatment is all that is required. It is advisable, however, to inspect the treated lesions for at least two days for signs of extension. If the crust is firmly fixed, which can be tested by grasping it with forceps, it must be left in place until it naturally separates after healing is complete.

FRAZIER, C. N. Prevention and cure of impetigo in infancy and childhood. *Chinese Med. J.*, 1936, June, 586-591.

LUPUS.

Lupus Erythematosus.—With a view to shedding some light on the aetiology of lupus erythematosus, CUMMER (Cleveland) secured statistics for a period of years from a clinic dealing with both white and negro patients. These showed a much higher incidence

among white persons, especially among those with other cutaneous affections. It is concluded that exposure to the sun's rays is a precipitating factor, and that pigmentation serves as a protective. The incidence of tuberculosis is much greater in the negro, and it is suggested either that there is no causal relationship between the diseases or that the intense pigmentation of the negro's skin serves as an offset in the case of lupus.

WRIGHT (Philadelphia) reports ten years' experience of treatment with gold and sodium thiosulphate. Of 76 patients so treated, 28 recovered, 26 were nearly cured, 13 were improved, and 9 failed to respond. Of those cured, nine have had no relapses for periods varying from four to seven years. When relapses occurred, further treatment usually caused the lesions to clear. The total dosage required for recovery varied from a minimum of 12 mg. in one case to a maximum of 2·175 gm. in another. Dermatitis occurred in eight cases.

LOMHOLT (Copenhagen) reports treatment of thirty-one patients with 'antileprol,' a preparation of the esters of chaulmoogra oil, used in the treatment of leprosy. The drug was given intravenously or intramuscularly in doses of 1 to 2 c.cm., an average of twenty injections being given. Eleven patients were cured, nineteen improved, and one unimproved. (*See also* Lupus Vulgaris.)

HOPKINS and BURKY (Johns Hopkins Hosp., Baltimore) report that patients with lupus erythematosus as a group react more intensely to staphylococcus toxin than do patients with other common cutaneous diseases. They suggest that the test may be of some aid in the diagnosis of questionable cases.

Lupus Vulgaris.—*BURNELL-JONES* (Royal Northern Hosp.) reports three cases in which tuberculin was used—one of lupus vulgaris of the face and two of lupus verrucosus of the hands. All three cases showed improvement and arrest of the disease. Whether tuberculin will cure lupus he cannot say definitely, but he advocates further trial. All three cases were of long standing, and one did not show improvement until after seven months' treatment.

AITKEN (Edinburgh) describes Lomholt's modification of Finsen's light treatment. The carbon in this lamp is set at an angle and the lenses are of fused silica which allows the arc to be placed nearer the lens. The time required for treatment is reduced to one hour and the results in many cases are amazing. Although his experience has not been long enough to judge of the permanence of the results, records by others point to a large percentage of permanent cures and very few relapses. This treatment has completely altered the outlook of sufferers from lupus vulgaris. MAYER (New York) says that of all forms of cutaneous tuberculosis, lupus vulgaris alone responds to actinotherapy. Lupus erythematosus does not respond and may be aggravated.

The similarity between leprosy and tuberculosis has led to trials of remedies for leprosy in cases of lupus vulgaris. Reports of such

trials record a certain amount of success, accordingly BURGESS (London) had prepared a mixture of the phenylethyl esters of a selected fraction of hydrocarpus oil (since put on the market as *Lulykol*), which he tried in eleven cases of lupus vulgaris Given intradermally in doses ranging from 0 25 to 2 0 c cm it cleared the patches rapidly and caused very little pain Clinical cure was effected in seven cases, the remainder were making satisfactory progress at the time of writing Burgess urges further trial of this remedy

As the result of a study of a number of chemical remedies, including salt brine, salicylic acid, copper sulphate, potassium permanganate, and pyrogallol, TISCHNENKO and co-workers (Kiew, U S S R) conclude that the most reliable is an ointment of pyrogallol, 10 to 20 per cent It is reliable, selective in its action, and gives generally satisfactory cosmetic results

Discussing the formation of keloids in relation to the treatment of lupus vulgaris, HELLIER (Leeds) suggests that lupus patients acquire an increased tendency to develop keloids Scraping the lesions and painting them with acid nitrate of mercury is an immediate cause of their formation, excision also favours it Treatment with the Kromayer lamp has much less effect, and creosote and salicylic acid have least effect of all Since keloid formation delays recovery, it is recommended that scraping and painting with mercury nitrate should be avoided An ointment of resorcinol, pyrogallol, and salicylic acid is recommended

AITKEN R Lupus vulgaris with special reference to its treatment with the Finsen Lomholt lamp *Edinburgh Med J* 1936 Mar 194 202 May (Trans Med Chir Soc) 57 68
BURGESS N Lupus vulgaris a note on a new method of treatment by intra dermal injection of phenylethyl hydnocarpate *B M J* 1935 Nov 2 835 837
BURNELL-JONES H S Tuberculin in the treatment of cutaneous tuberculosis *B M J* 1935 June 15 1212 1214
CUMMER C L Etiology of lupus erythematosus occurrence in the negro *Arch Derm & Syph* 1936 Mar 434 445
HELLIER F F The formation of cheloids in relation to the treatment of lupus vulgaris *Brit J Derm & Syph* 1936 Feb 91 96
HOPKINS H H and BURKY E L. Increased reactivity of the skin to staphylococcus toxin in patients with lupus erythematosus *Arch Derm & Syph* 1936 June 1060-1061
LOMHOLT, S Antileprolbehandlung bei Lupus erythematodes *Dermat Wschr*, 1935 July 6, 817 829
MAYER E Light therapy and roentgen therapy in tuberculosis present evaluation *J A M A* 1935 Nov 16 1599 1606
TISCHNENKO A M CLAUBERSON S A and FUKI M M Some chemical remedies for the topical treatment of lupus vulgaris *Urol & Cut Rev*, 1936 June 421 427
WRIGHT C S Ten years experience in the treatment of lupus erythematosus with gold compounds *Arch Derm & Syph* 1936 Mar, 413 433

NAEVI.

Dealing with the radium treatment of naevi, FINZI (London) remarks that this is one of the most successful of all medico-surgical treatments He stresses the importance of early treatment—during the first year of life if possible—and points out that its effect is slow

and continues for a year after application. Repetition is rarely necessary in less than six months, and then only if the effect is incomplete. Caustics should never be used. In all cases heavily screened gamma rays should be employed, and the dose should be such as to produce only a moderate erythema, otherwise scarring may result. With moderate dosage no after-effects are to be anticipated.

Finzi, N. S. The radium treatment of naevi *B.M.J.*, 1935, Sept. 28, 571-572.

NAIL AFFECTIONS.

Viecelli (San Francisco) reports a case of onycholysis, in which partial separation of the finger-nail from its bed was due to the patient's occupation, the handling of cowhides preserved in brine. Constant traction and softening of the nails and underlying tissue was evidently the cause: no fungus could be detected. The patient changed his occupation and in a month his nails began to assume a normal condition.

Heath (Birmingham) deals generally with dystrophic conditions of the nails attendant upon general diseases. He mentions grooving, transverse and longitudinal, hypertrophic thickening, pitting, etc. These conditions usually follow some illness, such as rheumatism, influenza, or septic tonsils, or they may accompany a skin disease like eczema or psoriasis. Nail dystrophy may be produced (*a*) by a direct toxic effect, limited as a rule to some of the nails, or (*b*) by a general nutritional depression, in which nearly all the nails are involved. Treatment in acquired dystrophic affections of the nails is likely to be successful only if a possible cause can be quickly discovered and removed. In cases of long standing a deformed nail, if exfoliated, is usually replaced by another of exactly the same type and habit of growth.

Heath, A. D. Dystrophic conditions of the nails seen with general diseases. *Med Press*, 1935, Sept 25, 281-284.
Viecelli, J. D. Onycholysis *Arch Derm & Syph*, 1936, Apr., 697-699.

PEMPHIGUS.

Pemphigus acutus.—Kerr (Birmingham) records a case of pemphigus acutus (butcher's pemphigus) which is of interest on account of the rarity of the condition. The patient was a young man engaged as a slaughterman, who had become infected at his work. His face and upper limbs were covered with vesicular and pustular lesions, from the fluid of which non-haemolytic streptococci were obtained. The larger blisters were removed and new vesicles were punctured as they appeared. A bland ointment consisting of lanolin (3) and olive oil (1) with 0·5 per cent. phenol was applied spread on muslin. Antistreptococcal serum (20 c.cm.) was injected intramuscularly on the third day, and when the temperature had settled permanganate baths were given. Recovery was rapid.

Pemphigus Neonatorum —CARTER and OSBORN (*Liverpool*) regard pemphigus neonatorum as the most important of a group of diseases comprised by the term neonatal dermatitis The lesion is situated under the epidermis and tends to spread centrifugally unless a reliable antiseptic is brought into immediate contact with the infecting organism The preventive method recommended by American workers of covering the new born infant with oil (see *PRESCRIBER 1934 Oct 321*) proved unsatisfactory Treatment must be undertaken while the affection is limited to the initial blister Pus is removed from the blister by means of a fine pipette and a 20 per cent solution of silver nitrate is injected into the evacuated blister An antiseptic dusting powder is then applied to the lesion This method was used with success in seventy four cases

Pemphigus Vegetans —BAILEY (Plymouth) reports a case in which cauliflower like masses were present on both legs and the patient was exceedingly anaemic Various treatments were tried including x rays ultraviolet rays organic arsenicals blood transfusion and germanin (Bayer 205) Under this last some improvement set in but the patient eventually relapsed and died Bailey thinks that this disease is usually fatal and that cases reported cured are to be regarded with suspicion as being either wrongly diagnosed or observed for too short a time

BAILEY K. C. A case of pemphigus vegetans with investigations and the effect of treatment upon it *Brit J Derm & Syph* 1936 July 370-377
CARTER H and OSBORN H A Neonatal dermatitis *BMJ* 1936 Mar 7 465 469
KERR I L A case of pemphigus acutus *Lancet* 1936 Mar 28 718 719

PIGMENTATION

Argyria —HARKER and HUNTER (London) report sixteen cases of occupational argyria seven generalized and nine localized Six of the workers showing the generalized condition had been employed for a number of years in the manufacture of silver nitrate the seventh was a maker of Christmas crackers The processes responsible for their disfigurement are now obsolete and have been replaced by methods of manufacture little likely to give rise to further cases The nine cases of the localized condition were silversmiths A detailed account is given of the processes involved in the factories where the patients worked the condition of the patients skins is described and the cases are recorded in detail

RAAF and GRAY (*Mayo Clinic*) report the case of a woman who had used a throat spray of silver proteinate for a number of years but eventually discontinued it Six months later she became pregnant with unusually severe vomiting and during this period she developed argyria over her entire body She gave birth to a normal child whose skin showed no discoloration It is suggested that the vomiting produced dehydration which caused a disturbance of metabolism and prevented the outgo of the ionic silver

Bismuthia.—LUETH and associates (Chicago) report a case of generalized discoloration of the skin, resembling argyria, following the prolonged use of bismuth by mouth. The skin was of a dark blue-grey colour and the oral mucosa a deep purple-black. The pigmentation developed after taking for over two years large doses of bismuth subnitrate for the relief of pain due to duodenal ulcer. Chemical analysis of portions of the skin showed that bismuth was responsible for the coloration.

Chrysocyanosis.—CARDIS and CONTE (Leysin, Switzerland) report thirty-four cases of skin pigmentation following the use of gold salts for tuberculosis. This relatively new disorder occurs more frequently in women than in men and most often in blondes, who are particularly susceptible. It is caused by the action of the sun's rays and is restricted to the exposed parts—face, neck, and hands. The colour may be ashy grey, mauve, or lilac, and is less dark than that due to silver. It may follow the use of any gold salt; it does not appear earlier than six months after the first injection, and it usually follows large doses. The condition is permanent and the only therapy is prophylactic: cases under treatment must be watched for the earliest signs of pigmentation. The colouring is unsightly, but otherwise harmless. [Some years ago Savy (*B.M.J.*, Nov. 24, '28, p. 962) reported a case of pigmentation due to sanocrysin plus sunlight, in which sodium thiosulphate was used with success.—See PRESCRIBER, 1929, Oct., 361.]

Iron Salts.—The use of ferric chloride as a lotion in the treatment of ivy poisoning (rhus dermatitis) in America has disclosed several cases of pigmentation through its use. TRAUB and TENNEN (Columbia Univ.) report several cases in which the iron has become fixed in the tissues causing a golden-brown pigmentation which appears to be permanent. They advise avoidance of lotions containing iron salts for any purpose.

Phenolphthalein.—*See* Dermatitis.

Vitamin C and Pigmentation.—HOFF (Konigsberg) thinks that the ascorbic acid (vitamin C) of the adrenals, or rather its deficiency, is responsible for the characteristic pigmentation of the skin in Addison's disease. Parenteral administration of ascorbic acid has been found to remove the pigmentation caused by sunlight as well as that sometimes associated with scurvy. The old practice of eating lemons to cultivate a pale complexion (when such was fashionable) is thus explained.

CARDIS, F., and CONTE, M. Chrysocyanosis (cutaneous pigmentation after injection of gold salts). *Annales de Derm. et Syphiligraphie*, 1936, Mar., 229.
HARKER, J. M., and HUNTER, D. Occupational argyria. *Brit. J. Derm. & Syph.*, 1935, Nov., 441-455.
HOFF, F. Klinische Beiträge zum Problem der krankhaften Hautpigmentierungen. *Dtsch. med. Wschr.*, 1936, Jan. 24, 129-134.
LUETH, H. C., and others. Bismuthia. *Arch. Int. Med.*, 1936, June, 1115; per *Lancet*, Aug. 22, '36, p. 445.

Pigmentation (*continued*) —

RAAF, J, and GRAY, H K Argyria becoming manifest in pregnancy *JAMA*, 1936 Mar 14 916

TRAUB, E F, and TENNEN, J S Permanent pigmentation following application of iron salts for the treatment of ivy poisoning *JAMA*, 1936, May 16, 1711-1712

PRURITUS.

Pruritus Ani.—Dealing generally with treatment, O'DONOVAN (London) says that for the simpler cases the anal skin may be painted with a solution composed of 1 per cent malachite green and 1 per cent mercuric chloride in 80 per cent alcohol, while a mixture containing potassium bromide 12 grains, aromatic spirit of ammonia 30 minims, oil of cajuput 2 minims, and infusion of valerian to half an ounce is given three times a day after meals This treatment will give complete relief in three weeks For more severe cases x-rays, one-third erythema dose, repeated in a fortnight and if necessary again a month later, will cure four-fifths of the patients Application of liquid tar is also useful, or chloral, camphor, and menthol (equal parts) may be rubbed on occasionally to afford relief

Many cases of severe pruritus ani exist for which no causative factor can be found, and in which ordinary treatment is ineffective For such cases HASKELL and SMITH (Philadelphia) recommend subcutaneous injection of 70 per cent alcohol A small portion of the skin is anaesthetized by injection of procaine hydrochloride, after which the alcohol is injected From four to six such treatments are necessary, requiring a quantity of 15-20 c cm of alcohol Of twenty-two patients so treated, sixteen secured complete relief and four were made comfortable No serious complications were encountered

Pruritus Vulvae.—RUST (Berlin) reports that he treated thirteen women suffering from severe pruritus vulvae with oestradiol benzoate (progynon-β oleosum) Complete relief was obtained in twelve cases All the patients suffered from ovarian insufficiency

HUNT (London) reviews 300 cases of pruritus ani and vulvae in which certain skin and other affections were found to be the underlying condition These are grouped as follows. general skin affections, chiefly lichen planus, 197, dermatitis, 59, local causes, 7, parasites, 3, constitutional disease (diabetes, anaemia), 15, psychic, 8, various, 11 It is pointed out that the great majority of these patients suffered from general skin affections, and the need for accurate diagnosis is thus emphasized

HASKELL, B, and SMITH, C D The subcutaneous injection of alcohol for pruritus ani *JAMA*, 1936 Apr 11 1248 1249

HUNT E Skin affections underlying pruritus of the vulva and anus a review of three hundred cases *Lancet* 1936 Mar 14 592 594

O DONOVAN W J Pruritus ani *Practitioner* 1936 Feb 148 158

RUST, W Zur Behandlung des Pruritus vulvae mit Follikelhormon *Münch med Wschr* 1936 July 31, 1273 1275

PSORIASIS.

While psoriasis is recognized clinically and histologically as an entity, a number of cases (about one in six) show associated conditions resembling fungus infection, etc MacKee and Foster (Columbia Univ) have made a study of biopsy specimens taken from typically psoriatic lesions of fifty patients They group the aberrant lesions and describe them, and their conclusion is that psoriasis cannot be unequivocally diagnosed from observations of a histological section *without considering the clinical findings The aberrant lesions link* psoriasis definitely as a fixed phase of a superficial dermatitis which may have the same aetiology as exfoliative dermatitis on the one hand or seborrhoeic dermatitis, eczema, etc, on the other The histopathological construction tends to change in conformity with the evolution of the clinical lesion The subject evidently calls for further study

Ingram (Leeds) reviews *thirty two cases of so called pustular* psoriasis This is characterized by small sterile pustules usually on the hands and feet, which dry to brown macules and are associated with scaling and erythema When the affection is associated with ordinary psoriasis elsewhere but is not itself generalized, the pustular phase often clears readily with rest and simple medication though the general psoriasis is stubborn In twenty of Ingram's cases there was no ordinary psoriasis elsewhere, and this group was resistant to treatment, in the early stages tar and x ray therapy were effective, but the later stages proved intractable In one case a resistant eruption in a woman cleared completely during pregnancy but relapsed immediately afterwards and has persisted since

Ellis (Baltimore) reports a case of psoriasis in which the condition was complicated by a unilateral superficial pustular eruption *after severe frost-bite of the hand The eruption had the features* which have been regarded as characteristic of acrodermatitis continua He concludes either that acrodermatitis continua is a form of pustular psoriasis or that the patient had had acrodermatitis continua previous to the development of psoriasis

Treatment—Little is known as yet of the aetiology of psoriasis, and treatment is consequently more or less empirical The result is a mass of literature in which various remedies have been advocated more or less enthusiastically The following are a few of the less usual remedies that have recently been advanced

Adrenal Cortex—Gruneberg (Halle) found extract of adrenal cortex of service in some cases, particularly those associated with arthritic symptoms, but it was by no means invariably effective Chrom (Denmark) reports only moderate success with the same treatment

Ascorbic Acid—Lutz (Basle) reports results with vitamin C or ascorbic acid It caused the eruption to disappear temporarily in three cases, although it had little effect in others He recommends a cautious trial in resistant cases

Colloidal Sulphur—THURMON (Boston) reports treatment with an organic compound of sulphur administered intravenously which gave gratifying remissions in fifty eight cases particularly in the more extensive cases The solution is of uncertain composition but is known to contain 2 mg of sulphur in each c cm in organic combination It is not recommended as a cure but rather as a means of control

Diet—DENEKE (Hamburg) discusses the dietetic treatment referred to last year (PRESCRIBER 1935 Oct 325) where it was suggested that the disease is due to abnormal lipoid metabolism He claims to have had good results from a diet low in fat and salt, with plenty of liquid and he gives a preparation of sarsaparilla at the same time

Irradiated Ergosterol—KRAFKA (Univ of Georgia) noticing that psoriasis usually cleared up under the summer sun tried the effect of vitamins A and D on a case of ten years standing Halibut liver oil with irradiated ergosterol was given in 3 minim doses twice daily, and within sixty days the patient s skin was quite clear The same treatment was tried in two other cases in one improvement was slow, and in the other the condition cleared but broke out again later

Parapsoriasis—The name parapsoriasis has been given to a group of rather uncommon maculopapular scaly dermatoses, including conditions known as parakeratosis variegata pityriasis lichenoides chronica dermatitis psoriasiformis nodularis and xantho erythro dermia perstans The name parapsoriasis has been regarded as unfortunate in that it suggests a relationship to psoriasis The essential lesion is a small inflammatory macule and the papules spread and coalesce forming guttate lesions small patches or a retiform pattern Their evolution is slow and prognosis is bad KULCHAR (San Francisco) reports two cases of the *en plaque* type treated with dioxyanthranol (cignolin Bayer) An ointment containing 0 25 per cent in soft paraffin was applied and in both cases the lesions cleared up completely A mild transitory erythema lasting a few days sometimes follows its use and pigmentation of the skin is frequently noted this last can be removed by a solution of xylol (40 per cent) in alcohol

CHROM S A Hormone from the suprarenal cortex in the treatment of psoriasis *Nord med t d krift* 1936 Jan 4 18 23
DENEKE TH Zur Allgemeinbehandlung der Psoriasis *Dtsch med Wschr* 1936 Feb 28 337 341
ELLIS F A Pustular psoriasis its relation to acrodermatitis continua vel perstans *Arch Derm & Syph* 1936 June 963 966
GRÜNEBERG T Ueber die Behandlung der Psoriasis mit Nebennierenrinden extrakt *Münch med Wschr* 1936 Apr 3 561 563
INGRAM J T Pustular psoriasis review of thirty two cases *Lancet* 1936 July 4 13 15
KRAFKA J A simple treatment for psoriasis *J Lab & Clin Med* 1936 Aug 1147 1148
KULCHAR G V Dioxyanthronal 1 8 in the treatment of para psoriasis *Urol & Cut Rev* 1936 Jan 38 39

LUTZ, W. *Einige Beobachtungen über die Beeinflussungsmöglichkeit der Psoriasis* durch Ascorbinsäure (Redoxon Roche) *Schweiz. med Wschr.*, 1935, Dec. 7, 1169-1170

MCKEE, G M., and FOSTER, P. D. Histopathogenesis of psoriasis and its aberrant lesions *Arch. Derm & Syph*, 1936, July, 35-56.

THURMON, F. M. The treatment of psoriasis with an organic sulphur compound *New England J Med*, 1935, Aug. 22, 353-358.

PURPURA.

ODDY (London), in a general article on the subject, remarks that a purpuric rash is a symptom that may be transient and of little importance or it may be the sign of a serious and even fatal condition. He classifies these cases in two groups—primary and secondary. Primary purpura includes (*a*) purpura haemorrhagica and (*b*) urticarial or anaphylactoid purpura (Schonlein's disease and Henoch's purpura). Secondary purpura is due to numerous causes, such as infection, chronic or toxic disease, or rupture of small blood-vessels. Treatment includes rest, nursing, iron and liver, blood transfusion, and splenectomy, according to the nature of the affection.

Discussing the possible allergic basis of the primary purpuras, BARTLEY and BELL (London) record twelve cases in children, of which six gave no history of any abnormality that could be regarded as suggestive of an allergic diathesis. The others showed histories of urticaria, migraine, asthma in the family, and digestive upsets with certain foods, but the purpura did not seem to be directly connected with these conditions. They conclude, therefore, that it is fallacious to label the primary purpuras as allergic.

GRAY (Glasgow) describes a case of Henoch's purpura which caused acute obstruction twice in eight days. The patient was a man aged 21, who for eighteen months had suffered from a purpuric rash. After fourteen days in hospital he developed severe colicky abdominal pains and vomiting. A congested appendix was removed and he made satisfactory progress for a week when the same pains again developed. The wound was reopened; much blood welled up and a gangrenous patch was found on the caecum. A lateral anastomosis between the ileum and the transverse colon was performed. The sickness stopped, the bowels moved naturally after a day or two, and the patient eventually recovered.

TOCANTINS (Cleveland) has investigated the blood changes occurring in thrombocytopenic purpura (p. haemorrhagica), having succeeded in producing the disease in dogs by intravenous injection of a specially prepared anti-platelet serum. The platelet count, he found, fell to below 50,000 per c.cm. within six minutes of injection. The mean bleeding time was definitely increased, and the coagulation time was at first diminished but later returned to normal. The clot retraction was also interfered with. The conclusion from his findings is that the mechanisms involved in purpura are more complicated than would at first appear.

The possibility of purpura being caused by drugs was mentioned

last year (PRESCRIBER 1935 Oct , 328) when several cases were cited in which the cause could be traced to gold or to arsphenamine A report by BOAS and ERF (New York) mentions two cases caused by hypnotics—one by phenobarbitone and the other by sedormid (allyl isopropyl allyl carbamide) In both cases the condition cleared up on discontinuance of the drug In the sedormid case the appearance of purpura coincided with the patient s menstrual period and it is pointed out that such coincidence may lead to the suspicion that an endocrine factor is responsible when the real cause is self-medication by the patient for the relief of menstrual pain

The value of moccasin snake venom for prognostic and therapeutic purposes is shown by the work of PECK, ROSENTHAL, and ERF (New York) The trend of the purpuric state can be determined by the persistence or otherwise of a positive skin reaction to the venom Successive intradermal injections are made of 0 1 c cm of a 1 3000 dilution of venom, with a control injection of 0 1 c cm of normal saline solution and the reaction is noted after an hour A positive reaction is indicated by capillary rupture with diffusion of blood into the tissues Change from a positive to a negative reaction indicates clinical improvement As a therapeutic measure in chronic purpura haemorrhagica subcutaneous injections of 1 c cm of 1 3000 venom given twice a week proved of value in twenty two out of thirty four cases in which it was tried The effect of such injections, together with the responses to the intracutaneous test indicate the prognosis of the disease and the necessity or otherwise of splenectomy

GWENDOLINE SMITH (London) reports a case of acute purpura haemorrhagica in which splenectomy was successfully performed the patient remaining in good health fifteen months after operation She concludes that this operation is certainly indicated in acute cases with severe bleeding and that delay in operating adds to the operative risks

In last month s issue page 291 mention was made of the discovery of a new vitamin P in lemon juice which proved effective in cases of decreased resistance of the capillary wall to whole blood—the vascular type of purpura haemorrhagica Given intravenously in daily doses of 40 mg this substance was found to restore capillary resistance and stop spontaneous bleeding within a fortnight

BARTLEY C H D and BELL, A D C The allergic basis of primary purpura in ch ldren *Lancet* 1936 Aug 15 359 361

BOAS E P and ERF L A Thrombocytopenic purpura following medicat on w th sedormid and v ith phenobarb tal *New York St J Med* 1936 Apr 1 491 494

GRAY T Henoch s purpura caus ng acute obstruct on twice in e ght days *Lancet* 1936 Apr 11 841

ODDY H M Purpura *Med Press* 1935 Oct 9 314 317

PECK S M ROSENTHAL, N and ERF L A The value of the prognost c venom react on in thrombocytopen c purpura *J A M A* 1936 May 23 1783 1791

SMITH G Splenectomy for thrombocytopenic purpura *B M J* 1936 Jan 25 157 158

TOCANTINS L M Experim ental thrombopenic purpura in the dog *Arch Path ol* 1936 Jan 69-78 ——Experimental thrombopenic purpura cyto log cal and physical changes in the blood *A n Int Med* 1936 Jan 838 849

SCABIES

KINGSTON (Wakefield) describes an outbreak of scabies in a mental hospital, where one of the difficulties of treatment is the failure of the patient to co-operate Sulphur ointment having proved unsatisfactory, a combination of sulphur and turpentine was tried Thirty grains of sulphur was heated in a test tube, oil of turpentine was then added in small portions, boiled, and decanted, until all the sulphur was dissolved, six ounces being used Two ounces of liquid paraffin was then added the resulting solution being a clear amber fluid containing about one per cent of sulphur This was applied on three successive days While it was found to be superior to sulphur ointment, it did not prove ideal, being suited only to a certain type of patient Of twenty three cases so treated, nineteen were cured after one or two courses, three more after three courses, and the remaining case was cured with mitigal a 'Bayer' product of organic sulphur

The inconvenience of the time honoured sulphur treatment has led to the introduction of several new methods KULCHAR and MEININGER (San Francisco) find that the precipitation of colloidal sulphur on the skin by the interaction of a 40 per cent aqueous solution of sodium thiosulphate and a 4 per cent solution of hydrochloric acid provides a simple, effective and economical treatment The thiosulphate solution is applied over the entire body, fifteen minutes later the acid is similarly applied, and an hour later the process is repeated This is done on two successive days In their experience this is superior to the Danish method (an ointment of sulphides of potassium) and results in a higher percentage of cures and a lower incidence of dermatitic reactions

KISSMEYER recommends the use of benzyl benzoate, the constituent of balsam of Peru which he believes to be the active agent The patient is well washed in a warm bath, the whole body is then brushed over with a mixture of equal parts of benzyl benzoate, alcohol and soft soap, and as soon as this is dry the process is repeated The patient resumes his clothes, takes a bath twenty four hours later, and then changes his under linen which can be washed without disinfection

SWEITZER and TEDDER (Minneapolis) advocate the use of pyrethrum ointment This consists of an absorbent fatty base containing an extract of pyrethrum flowers, 100 gm representing 83 gm of the flowers The ointment is applied over the body after a hot bath and the process is repeated on successive days Cure usually results in from five to seven days

KINGSTON F E An outbreak of scabies in a mental hospital *Lancet* 1935 Oct 12 815 817
KISSMEYER A Le traitement de la gale par le benzoate de benzyle *Bull méd Paris* 1935 Nov 23 821 822
KULCHAR, G V and MEININGER, W M Sodium thiosulfate in treatment of scabies *Arch Derm & Syph* 1936 Aug 218 219
SWEITZER S E and TEDDER J W Pyrethrum in the treatment of scabies *Minnesota Med* 1935 Dec 793 795

TULARAEMIA.

The disease known as tularaemia was described in these pages fourteen years ago (PRESCRIBER, 1922, June, 201) at the time it first attracted serious attention. It is due to infection by *Bacterium tularense* (*Pasteurella tularensis*, named after Tulare, a district of California), and is a plague-like malady infecting rabbits and other rodents, from which it is conveyed to man by insects, the blood-sucking horse-fly *Chrysops discalis* being chiefly responsible. Originating in the United States, it has been found also in Japan and in Russia, but so far it has not been reported from other countries. The most frequent clinical form is the ulcero-glandular type, which begins as a lesion of the skin. The lymph glands draining the bitten area become inflamed and frequently suppurate. The fever is of a septic type, lasting from three to six weeks. The disease affects chiefly workers on the land, but others may be infected by insects. It is apparently non-contagious. Diagnosis is simple: agglutination and isolation of the organism are sufficient.

AMOSS and SPRUNT (Durham, North Carolina) report two fatal cases in which the disease was evidently contracted through eating rabbit. Although they cannot prove that the rabbit was infected, it seems likely that it was, also that it was not well cooked, and that the organism entered the system by way of the alimentary canal. There was no doubt regarding the diagnosis of tularaemia, though only one patient gave a positive agglutination to *B. tularense*. BERNSTEIN (U.S.A.) reports three fatal cases in all of which the patients showed signs of lung involvement. At necropsy in each case caseous nodules were found in the lymph nodes, lungs, liver, and spleen. WRIGHT (Alberta) reports two cases occurring in Canada Both patients had handled and skinned rabbits. The symptoms were not severe and suggested less serious conditions, but both gave positive agglutinations to *B. tularense*. Both patients recovered. SLOAN and associates (Chicago) report a case of tularaemic pneumonia complicated by a spontaneous hydropneumothorax. Supportive and palliative measures resulted in recovery. A fatal case of tularaemic pneumonia, with associated ileitis, is reported by FETTERMAN and LERNER (Pittsburgh). It is believed that the organism found entry by the respiratory tract.

FLINN (Wilmington, Delaware) cites two cases treated with the first antiserum commercially available. The first case was of the ulcero-glandular type: 30 c.cm. was given on the eighteenth day of the disease and the patient was well six weeks after the onset. The second case was of the severe pneumonic type: 90 c.cm. on the fourteenth day effected recovery; relapse set in after two months, but this subsided immediately following 30 c.cm. of serum.

AMOSS, H. L., and SPRUNT, D. H. Tularemia: review of literature of cases contracted by ingestion of rabbit and the report of additional cases with a necropsy. *J.A.M.A.*, 1936, Mar. 28, 1078-1080.

BERNSTEIN, A. Tularemia: report of three fatal cases with autopsies. *Arch. Int. Med.*, 1935, Dec., 1117-1135.

FETTERMAN G H and LERNER, H A fatal case of tularemic pneumonia with associated ileitis *J Lab & Clin Med*, 1936 Aug 1157 1161
FLYNN L B Specific anti-serum in treatment of tularemia two unusual cases treated successfully with commercial anti serum *Delaware St Med J*, 1935 Nov 219 222
SLOAN, L H, FREEDBERG, A S, and EHRLICH, J C Tularemic pneumonia *J.A.M.A* 1936 July 11, 117 119
WRIGHT, E K Two cases of tularaemia *Canad Med Assoc J*, 1935, Sept, 309-310

ULCERS.

Leg Ulcers.—ALKE (Bad Meinberg) describes his treatment as follows To remove the eczema, Wilkinson's ointment is rubbed on with a wooden spatula daily for a week The ulcer is then cleaned with benzol, after which resorcinol powder is applied and the part covered with an adhesive bandage This is repeated weekly for several weeks, by which time healing usually results Should the ulcer persist, x-rays are applied For after-treatment the area is massaged daily for several months with Wilkinson's ointment until all scales have disappeared If this is properly done cure is usually permanent [Wilkinson's ointment contains sulphur 1, tar 1, potash soap 2, benzoated lard 2, talc 0 5]

Some years ago (PRESCRIBER, 1931, Feb , 69) the local application of insulin in the treatment of leg ulcers was reported to have been very successful Following these reports, SCHWEITZER (Fiume) states that he has treated two cases of ulcus cruris by dropping on insulin, and noted a definite acceleration of healing He has also used an ointment containing pancreatin with zinc oxide, lanolin, and cod-liver oil, and a powder consisting of pancreatin, zinc oxide, starch, and talc With these preparations he has treated with success six cases of leg ulcer, as well as other skin diseases , one of the cases of leg ulcer was of long standing

Tropical Ulcer.—In a series of five articles, BROWN discusses the ulcer syndrome in tropical Africa Ulcers may be phagedenic or non-phagedenic the latter, which are due to trauma, etc , may become phagedenic later He believes that a strong correlation exists between the phagedenic type and *Bacillus fusiformis* and *Spironema* in 423 cases 53 9 per cent showed either or both of these organisms and in 89 per cent of these the ulcers were phagedenic The presence of these organisms in a non phagedenic ulcer indicates a change to phagedenic For treatment he first uses ordinary local measures and a standard hospital diet , if progress is *not satisfactory, calcium chloride is given intravenously 1 gm in* 10 c cm of water once or twice daily Should the ulcer still persist, parathyroid extract is given orally Many patients with phagedenic ulcers have a low calcium level or parathyroid insufficiency ; this is due to faulty diet, the patients being mostly vegetarians

DALE (West Africa) uses a paste called ' Zipp,' which consists of zinc oxide 1, iodoform 1, soft paraffin 2 This is applied on gauze, covered with several thicknesses of gauze with a plaster of Paris

bandage over all, and left for three weeks or longer. By this time the ulcer is usually found to be healed.

ALKE, Dr. Die Behandlung der Ulcera cruris *Münch med. Wschr*, 1936, Feb. 14, 270-271.
BROWN, A. A. F. The ulcer syndrome in tropical Africa. *J. Trop Med*, 1935, July 1, 157; July 15, 170; Aug 1, 187; Aug 15, 201; Sept 2, 215
DALE, W. C. "Zipp" treatment of ulcers. *West African Med. J.*, 1935, Nov, 16-17.
SCHWEITZER, A. The external application of pancreas hormone in dermatology with special reference to the treatment of ulcus cruris and roentgen ulcer. *Urol & Cut. Ret*, 1936, May, 333-335.

URTICARIA.

From experimental evidence it seems probable that deficient elimination of histamine plays an important part in the production of recurrent urticaria. On this assumption FIESSINGER and GAJDOS treated six cases by ionization with histamine, and in all cases complete cessation of the urticaria resulted. A compress moistened with a 1 : 10,000 solution of histamine hydrochloride was placed over the epigastrium and covered with an aluminium plate, which was connected with the positive pole, the negative pole being held in the patient's hand. A current of 6 to 10 milliamperes was passed for five to ten minutes. As many as twelve treatments may be necessary on alternate days. The treatment was found to be unsuitable for pruritus from other causes.

FIESSINGER, N, and GAJDOS, A La réactogénothérapie de l'urticaire récidivante par l'ionisation à l'histamine *Presse méd*, 1935, Nov 27, 1913-1914

VARICOSE VEINS.

The cutaneous complications of varicose veins have hitherto been regarded as the result of chronic passive congestion of the skin and subcutaneous tissues caused by venous stasis in the varicose vessels. ZIMMERMAN (Chicago) is not satisfied with this explanation, which he regards as incompatible with the clinical features. By means of infra-red photography he has been able to demonstrate an immediate topographical association of varicose eczema and ulcer with subjacent dilated trunks. He concludes, therefore, that the cutaneous lesions are not the result of chronic passive congestion, but are of inflammatory origin, arising through direct extension from infections within the varicosities.

SAYLOR and associates (New York) report the treatment of twenty-six cases of chronic varicose ulcer by ionization with acetyl-β-methylcholine chloride. Asbestos paper saturated with a 0·5 per cent. solution was applied to the leg and a metal plate placed over it (but not on the ulcerated area) and connected with the positive pole. The negative pole was connected with an electrode placed on the patient's back. A current of 20-30 milliamperes was used, and treatment was given daily or twice or thrice weekly for twenty minutes. Results were satisfactory in all but three cases.

SAYLOR L KOVACS J DURYEE A W and WRIGHT I The treatment of chronic varicose ulcers by means of acetyl beta methylcholine chloride iontophores s *J.A.M.A* 1936 July 11 114 117
ZIMMERMAN L M Pathogenesis of the cutaneous complications of varicose veins *Arch Derm & Syph* 1936 July 97 102

WARTS

For the electric removal of warts and moles from the face some kind of local analgesia is necessary but injection of procaine, etc, is painful and is apt to distort the field of operation McLAUGHLIN (New York) has found that application of trichloracetic acid is free from these disadvantages The acid is applied full strength to the surface of the lesion, a toothpick or other applicator being used The lesion should be surrounded with soft paraffin to protect the adjacent skin After a minute or two when the painted area is thoroughly whitened sufficient analgesia will have developed to permit light interrupted desiccation, this will increase the analgesic effect until a moderately strong current can be used

GHOSH and MAPLESTONE (Calcutta) report treatment by injection of an emulsion made from wart tissue The patient s warts are sterilized by application of alcohol and ether and carefully removed, a known weight of wart tissue is ground up with pumice stone powder until it makes a uniform emulsion with normal saline solution This is incubated at 37° C for twenty four hours filtered and mixed with saline containing 0 25 per cent formaldehyde Injections of 0 2 c cm of this emulsion, gradually increased to 1 c cm, are given subcutaneously or intradermally twice weekly from six to twelve injections usually being sufficient This treatment gave good results in seventeen cases of infective warts and in twelve cases of plane warts For papillomatous warts it proved ineffective

PRITCHER (New York) describes his treatment of plantar warts as follows The site of the wart is washed with alcohol ether A piece of carbon dioxide snow is applied until the entire area is blanched Then the monopolar current is used to desiccate the surface of the wart until the patient complains of pain The carbon dioxide snow is reapplied with slight pressure and the lesion is desiccated once more This is repeated until slight bleeding of the wart is noticed The edge of the wart is then gently raised with a scalpel and the entire wart comes away, leaving a slightly oozing base The bleeding points are desiccated with the same current and a pressure dressing of gauze is applied The dressings are changed every other day and usually in about a week the wound is healed

GHOSH L M and MAPLESTONE P A Infective warts and the r treatment *Ind an Med Gaz* 1935 Aug 441 444
McLAUGHLIN R R M Treatment of moles and verrucae trichloracet c acid as an analgesic agent *New York St J Med* 1936 Mar 1 347 350
PRITCHER J L Plantar warts a simple method of treatment *Arch Derm & Syph.* 1935 Dec. 923

USEFUL SKIN PRESCRIPTIONS.

The following prescriptions have in most cases been selected from the literature of the past few years as presenting features worthy of notice They have been carefully revised in accordance with the nomenclature of the British Pharmacopoeia (1932) and British Pharmaceutical Codex (1934), and in most cases the metric equivalents are given along with the imperial weights and measures

CONTACT DERMATITIS

Protective Film

℞

Ivory soap flakes			7 48
Glycerin, pure			26 40
Sodium silicate			24 20
Tragacanth			0 21
Oil of lemon			0 16
Water			41·60

This forms an invisible protective film, soluble in water and non irritating to the normal skin Applied to the hands it permits of working with substances likely to cause irritation

Cook County Hosp *J.A.M.A*, Dec 21, '35, p 2064

FUNGUS INFECTION OF THE FEET

℞

Acidi benzoici		25 gr	1 6 gm
Acidi salicylici		15 gr	1 0 gm
Paraffini mollis		120 gr	8 0 gm
Paraffini duri		15 gr	1 0 gm
Olei cocois	ad	1 oz	30 0 gm

Misce, fiat unguentum (This is a modification of Ung Acid Benz Co, B P C, or Whitfield's ointment)

℞

Acidi benzoici		90 gr	6 0 gm
Acidi salicylici		60 gr	4·0 gm
Acetoni		1 fl oz	30 0 ml
Spiritus methylati industrialis	ad	4 fl oz	120 0 ml

Misce, fiat pigmentum (This may be used in place of, or alternated with, the foregoing)

℞

Cupri nitratis		40 gr	2 6 gm
Acidi benzoici		90 gr	6 0 gm
Acetoni		1½ fl oz	45 0 ml
Spiritus methylati industrialis		5½ fl oz	170·0 ml
Aquam	ad	8 fl oz	250 0 ml

Misce, fiat lotio Signetur 'Apply twice daily'

M Sydney Thomson *Med Press*, Mar 4, '36, p 205

PRURITUS

℞

Mentholis		4½ gr	0 5 gm
Spiritus rectificati		45 m	5 0 ml
Talci purificati		2 oz	100 0 gm

Misce, fiat pulvis Signetur 'Use freely as dusting powder'

PRURITUS (*continued*).

℞

Mentholis	¼ gr.	0·015 gm.
Acidi borici	150 gr.	10·000 gm.
Aquae	16 fl oz.	500·000 ml.

Solve; fiat lotio. Signetur: 'Apply on gauze compress.'

℞

Mentholis	5 gr.	0·3 gm.
Phenolis	10 gr	0·6 gm.
Unguenti aquae rosae (B.P.C.)	1 oz	30·0 gm.

Misce; fiat unguentum. Signetur: 'Apply locally as required to prevent scratching.'

Cook County Hosp.: *J.A.M.A.*, June 20, '36, p. 2145.

PSORIASIS.

℞

Liquoris picis carbonis	60 m.	4·0 ml.
Hydrargyri ammoniati	10 gr.	0·6 gm.
Unguentum paraffini ad	1 oz.	30·0 gm.

Misce; fiat unguentum.

J. A. Drake: *Practitioner*, May '36, pp. 601-602.

RINGWORM OF THE SCALP.

℞

Iodine crystals	60 gr	4·0 gm.
Tri-ethanolamine	60 gr	4·0 gm.
Goose grease	1 oz.	30·0 gm.

When mixing this prescription do not add the tri-ethanolamine to the iodine, but mix the iodine into the goose grease and then add the tri-ethanolamine with as little friction as possible. The reaction between tri-ethanolamine and iodine is violent, but in the presence of goose grease a slow change takes place. The preparation should be dark brown and should be kept as cold as possible when not in use. When it becomes the colour of chicken fat, which takes place in about ten days, the ointment is less effective.

M. T.-R. Maynard *Arch. Derm. & Syph.*, Aug. '36, p. 268.

THERAPEUTIC ABSTRACTS.

Treatment of Dysmenorrhoea.—Painful menstruation, according to PHILLIPS (London), may be due to several causes. It may be due to structural defects, such as a small uterus; it may be of endocrine origin, as in the stout, lethargic type of patient; debilitating conditions such as anaemia, tuberculosis, or lack of muscle tone predispose to it, in which cases physical exercises are beneficial; or it may be neurotic or neuro-muscular. In cases of endocrine origin small doses of dry thyroid night and morning for a week prior to the period are often successful. Some cases respond well to the gonadotropic hormone of the anterior pituitary. Treatment by medicinal agents other than hormones is purely palliative, but as such is often valuable. Among the drugs recommended are viburnum, apiol, pulsatilla, bromides, phenazone, and atropine.

PHILLIPS, L. The treatment of dysmenorrhoea. *Med. Press*, 1935, Dec. 4, 493-498; Dec. 11, 514-518; Dec. 18, 536-540.

Carbon Dioxide in Acute Alcoholism.—According to ROBINSON and SELESNICK (Boston), in acute alcoholic coma with dangerous respiratory depression, paralysis, and cyanosis death may be definitely prevented and recovery accelerated by inhalation of a mixture of carbon dioxide (10 per cent) and oxygen (90 per cent). Inhalation should be continued long enough to establish and maintain normal respiration and colour after the inhalation is suspended: the minimum period is half an hour. The purpose of this treatment is not to arouse completely a comatose alcoholic patient but to reduce him from a state of dangerous paralytic alcoholism to the less deep stage of anaesthesia from which he can safely be expected to recover. The method is recommended as an emergency treatment only: it is not intended to apply to the moderately intoxicated person more frequently encountered.

ROBINSON L. J. and SELESNICK S. The treatment of acute alcoholism with ten per cent carbon dioxide and ninety per cent oxygen inhalation. *J.A.M.A.* 1935 Nov. 30. 1734–1738.

Toxaemias of Pregnancy and Diet.—THEOBALD (London) reports certain results which may be held to support the dietetic-deficiency hypothesis of the toxaemias of pregnancy. Five patients, in the later weeks of pregnancy, suffering from a symptom-complex due to nervous lesions and usually described as gestational neuritis, were cured by dietetic treatment. The symptoms in four cases were completely relieved merely by the addition of vitamin B_1 to their dietaries, and it is assumed that the symptoms resulted from a deficiency of that substance in the diets. Two patients suffered in addition from deficiency of vitamin D in their diets. The term 'atelositetic neuritis of pregnancy' is suggested for this form of neuritis from the Greek ατελης (imperfect) and σιτησις (nutrition).

THEOBALD G. W. Neuritis in pregnancy successfully treated with vitamin B_1. *Lancet* 1936 Apr. 11. 834–837.

Pentothal-Sodium in Mental Cases.—HORSLEY (Dorset Mental Hosp.) describes pentothal sodium (see PRESCRIBER, Apr. '36, p. 122) as a new and powerful narcotic of particular value in mental cases. It has been administered to patients of all ages from 20 to 75 years. The intravenous route has widest application: a 10 per cent. solution is injected in doses of 10 c.cm. at a rate not exceeding one c.cm. per minute. For narco-analysis a 2·5 per cent. solution is more convenient. When used to counteract mania a larger dose must be given, and the injection should be continued until deep surgical anaesthesia is produced, whereupon a further dose is injected intramuscularly. This ensures a deep sleep for about an hour, with a subsequent period of lighter sleep for several hours if the patient is undisturbed. Pentothal sodium is effective also when given orally or by rectal injection.

HORSLEY J. S. Pentothal sodium in mental hospital practice. *B.M.J.* 1936 May 9. 938–939.

NEW REMEDIAL AGENTS.

Vitamin E in Habitual Abortion

THE possible use of wheat germ oil (vitamin E) in the treatment of habitual abortion in women was mentioned in these pages a few years ago (PRESCRIBER, 1932, Feb , 52) Since then several reports have been published WATSON (London, Ontario) has tried it in a number of cases and concludes that, while a definite decision regarding its therapeutic value must be reserved pending further observations, there is evidence that vitamin E plays a part in the promotion of gestation, and that wheat germ oil offers promise of being beneficial in the prevention of habitual abortion and probably also in the treatment of threatened abortion It is of no avail in the treatment of non fertility

During the past two years CURRIE (Univ of Leeds) has treated twenty nine cases of habitual abortion with a concentrate of vitamin E (wheat germ oil extract) The results were as follows twenty-three of the women have been delivered, and the other six are all past the sixth month of pregnancy Twenty two living children were born , one of these died of a structural deformity, and one case ended in abortion The twenty three delivered mothers had, collectively, seventy three previous pregnancies, resulting in only eleven children five of whom died immediately after birth The average treatment lasted five months One capsule of wheat germ oil extract (Glaxo) was given daily , these capsules contain three minims of extract, equal to about 75 minims of the oil

CURRIE D W Vitamins for habitual abortion *B.M.J* 1936 Apr 11 752
WATSON E M *Clinical experiences with wheat germ oil (vitamin E)* *Canad Med Assoc J* 1936 Feb 134 140
WATSON E. M and TEW W P Wheat germ oil (vitamin E) therapy in obstetrics *Amer J Obstet & Gynec* 1936 Feb , 352 358

New Drugs and Preparations.

[Under this heading are given brief notices of new non secret products as they appear on the market or are mentioned in medical literature The notes are intended for reference only and must not be taken to imply anything in the nature of a recommendation In most cases the information is derived wholly or mainly from makers advertisements]

Dmelcos —A diagnostic vaccine containing 450 million *B ulceris cancrosi* (Ducrey) in 1 c cm. of normal saline For intracutaneous test of infection by Ducrey bacillus in doubtful cases of soft chancre and bubo Positive result shown by appearance of a papule with erythema in two days time Ampoules 0 25 c.cm. (May & Baker Ltd Dagenham)

Eldoral (Heyden) —A synthetic hypnotic in which an ethyl group of barbitone is replaced by a piperidine group Its action is less than that of other barbiturates because of its low solubility, and it is said to be safe and effective in doses of 0 25 gm (4 grains) —Gros Gielen *M m W* Jan 17, 36 pp 93-95

Epokan (Merck)—A preparation for the treatment of asthma, containing a compound of ephedrine and coumarin with other ingredients to aid its antispasmodic effect—Kreitmair Laechele *M m W*, Jan 24, '36, pp 139 142

Kephrine Hydrochloride—The monohydrochloride of a base resembling adrenaline, but differing in having a ketone group in place of the secondary alcohol group Acts as vasoconstrictor, less powerful than adrenaline but its effects are more lasting No appreciable absorption, hence no rise of blood pressure Used locally to arrest capillary bleeding (Pharm. Indust A.-G., Vienna)—*J A M A*, July 25, '36, p 282

Leucarsone.—Para carbamino phenylarsonic acid, containing 29 per cent As Known in America as *Carbarsone* For treatment of amoebic dysentery, colitis, and other intestinal infections Tablets 4 grains (0 25 gm), dose, one tablet twice daily (May & Baker Ltd, Dagenham)

Neko—A germicidal soap containing 1 per cent mercuric iodide, for use as an antiseptic detergent, the saponaceous base assisting the action of the mercuric salt An effective bactericide and parasiticide for the skin, capable of many applications Coloured blue for distinctiveness, and supplied in tablets, or as soft soap in collapsible tubes (Parke, Davis & Co)

Planacrine—Lozenges each containing 3 mg of euflavine, flavoured with glycyrrhizin and peppermint Combat infection and relieve pain in sore throat, tonsillitis, and other mouth and throat affections One is allowed to dissolve in the mouth as required two can be taken per hour, or 20 in 24 hours Colour saliva and mucous membrane yellow (May & Baker Ltd, Dagenham)

Tanna flavine—A mixture of tannic acid and acriflavine in powder form, issued in tubes containing sufficient to prepare half a pint of 2 5 per cent solution of tannic acid with acriflavine, for application in severe burns *Tanna flavine Jelly* is a non oily preparation of tannic acid and acriflavine, in collapsible tubes for treatment of minor burns and as a first aid measure in severe burns (British Drug Houses Ltd, London)

Veracolate—A combination of bile salts with aperients in tablet form, containing sodium glycocholate and taurocholate with cascara sagrada, phenolphthalein, and capsicum The combination acts as a cholagogue and evacuant and is indicated in biliary stasis, intestinal fermentation, hepatic insufficiency, after cholecystectomy, and in biliary disorders generally Dose, one to three tablets on retiring or one tablet after each meal (William R Warner & Co Ltd, London)

The Energen Foods Co Ltd (Bridge Road London N W 10) have issued a little 32 page DICTIONARY OF DIETARIES for the use of medical men It gives specimen menus for a number of conditions with notes of the dietary essentials in each case and the information has been compiled after consultation with a number of well known authorities in dietetics whose names appear at the end of the book Further the Service Department of this firm is prepared to supply physicians with (*a*) standard diet charts for any purpose (*b*) a specially planned dietary for an individual patient on particulars being furnished and also to supply panel patients and others whose means necessitate it with Energen bread and foods at reduced prices Suitable applicat on cards for making these requests are available and we commend this useful service to our readers

REVIEWS OF BOOKS.

Vitality and Energy in Relation to the Constitution By T E Hammond, F R C S Pp 314 (H K. Lewis 12s 6d)

In this book Mr Hammond has attempted to solve a problem frequently met in general practice—want of vitality in the patient No disease is detectable, but the condition is so marked that neither work nor play can be enjoyed When such a patient is subjected to undue stress or strain there is a tendency to organic disorder or to the manifestation of some infective invasion, Mr Hammond therefore sets himself the task of defining vitality, the lack of which makes for so much ill health and predisposition to disease He holds that there is a centre for energy as well as for basal and psychological functions, and that the function of all the vital organs is concerned with the maintenance of this centre He believes this centre to be situated in the basal ganglia, the centre of tonus of the muscular organs and skeletal muscles is situated in the mid brain and is under control of the basal centre of vital energy Mr Hammond grapples with his subject through fifteen chapters, but somehow he does not seem to solve the problem of vitality The chapters, though somewhat disconnected in places, are well written and show a profound sympathy and a wide experience of life and living in health and in sickness He is inclined to be mildly cynical about the aimlessness of research which neglects the principles of medicine Indeed one feels inclined to agree with him when he says 'the advance of knowledge is taking place so rapidly that it is becoming increasingly difficult to grasp what the others are talking about' J I

Euthanasia and Other Aspects of Life and Death By Harry Roberts Pp 298 (Constable 7s 6d)

That old crusader, Dr Harry Roberts, idealist, equalitarian, and sociologist, gives us yet another volume of entertaining essays He deals not only with euthanasia and suicide, but also with such fundamentals as love and sex, crime and punishment, education and the child, and the sterilization of the unfit The remarkable thing about the book is that a writer famous for decided views should, on this occasion, appear so judicial, so impartial, and apparently so fearful lest he should fail to provide all the pros and cons He makes it quite clear that on so many of the questions he discusses there is only one body in the world to day which gives an unequivocal lead—the Catholic Church While he and the rest of us are discussing with dubiety and without conclusion the rights and wrongs, for example, of euthanasia, sterilization, divorce, and much else, this one authority says it knows, and not only knows but also claims to provide guidance The thinking man, whether Catholic or otherwise, will read this volume of controversial matter with gusto, and perhaps because of its scientific impartiality will begin to think anew The best chapter is entitled 'Education and the Child' It embodies a ripe wisdom which will appeal to all who love children R. C O

The Vegetative Nervous System A Clinical Study By Wulf Sachs, M D Pp 168 (Cassell 15s)

This is a comprehensive review of an increasingly important subject A first reading rather takes one's breath away the author is evidently

so full of his subject that the reader has difficulty in keeping pace with him, and several readings are necessary to do justice to his work He goes very deeply into the clinical aspect, especially as regards tests for sympathicotonia and parasympathicotonia, and he has evidently done a large amount of clinical work on these lines His action in publishing his investigation is praiseworthy, and the book, and especially the diagrams, will form a valuable route map for those who follow him At the moment one has difficulty in placing a true value on his findings, but this does not in any way detract from his enthusiasm, skill, and knowledge, and clinicians will find much food for thought in his pages Schiff's words are endorsed 'the part played by the autonomics in regulating the internal processes of the organism is not so simple as would appear theoretically it is a living anatomical reality which is fundamental to the whole of physic' J O

The Relief of Pain A Handbook of Modern Analgesia By Harold Balme, M D, F R C S Pp 392 (Churchill 12s 6d)

Writing from a wide experience and with maturity of judgment, Mr Balme has presented this important subject in an exceptionally attractive manner Pain in the abstract is considered in its various aspects, anatomical, physiological, and psychical all in the light of the most recent literature, then comes a study of the clinical significance of pain as a symptom and its appropriate treatment in individual cases The author succeeds in presenting to his readers a very wide review of clinical medicine and surgery—and even obstetrics—where pain is a salient feature, so that when the volume is laid down one feels that ere long it will be picked up again and some chapters will be re-read and all will be consulted at some time or other An excellent and most praiseworthy treatise J O

Hints to Probationer Nurses in Mental Hospitals By Richard Eager, *O.B.E*, M D Third Edition Pp 222 (H K Lewis 8s 6d)

This edition of Dr Eager's book has been extended to a volume of 222 pages, and contains a great deal of additional matter based upon the author's long experience of asylum practice The work is essentially practical, and includes chapters on ward duties, psychology, dreams, and the various forms of mental disease The clinical symptoms are given in simple language and we are glad to note that many of the new terms peculiar to psychology are either omitted or, if used, carefully explained. The book can be strongly recommended to the nursing staff of mental hospitals D O

British Masters of Medicine Edited by Sir D'Arcy Power. Pp 242 (Medical Press and Circular 7s 6d)

Here are two dozen short biographies of eminent British physicians from Harvey to Starling, written by as many authors, all of them well known to medicine or science, and identifiable by initials at the end of each article The book's brevity makes it appropriate to the curiosity of the layman rather than to the instruction of the practitioner, who, however, will find entertainment in abundance within its covers Much matter that if not new, is at least being lost sight of, is brought into fresh prominence For example there is the dramatic story of Hugh

Owen Thomas, a general practitioner of whom it has been said that his chief contribution to surgery was Sir Robert Jones. He and not Jones was the father of orthopaedic surgery as Jones generously admitted. Thomas was Jones's uncle and teacher. His posthumous fame rests upon tributes made chiefly by Sir Robert. An excellent chapter is concerned with the extremely attractive personal character of Sir William Osler. Simpson and Lister respectively receive adequate if brief treatment, as do many others. R. C. O.

MEDICAL RESEARCH COUNCIL SPECIAL REPORTS.

No. 210. Bacterial Nutrition. By B. C. J. G. Knight, M.Sc. (H.M. Stationery Office. 3s.)

A knowledge of the conditions governing the growth and multiplication of bacteria is essential to a better understanding and control of infectious diseases. With this object in view the Medical Research Council has established a special department for research in bacterial chemistry. Mr Knight, who is one of the Council's scientific staff, devotes the main part of this report to a systematic survey of all available information on the subject of bacterial nutrition. These data are then dealt with in the light of the hypothesis that the different types of nutritive requirement exhibited by bacterial species represent successive levels in an evolutionary scale, and it is further shown how bacteria can adapt themselves to changes in their nutritional environment.

No. 211. The Influence of Diet on Caries in Children's Teeth. (H.M. Stationery Office. 2s.)

This is the final report issued by the Committee on Dental Disease, whose interim report was published in 1931. It fully confirms the results published by Mrs Mellanby, which showed that the presence of vitamin D in the diet definitely reduces the incidence of dental caries in children. This result was particularly noticeable when the vitamin diet was given during the period of development and before full eruption of the teeth.

No. 212. Investigations on Respiratory Dust Disease in Operatives in the Cotton Industry. By Carl Prausnitz, M.D. (H.M. Stationery Office. 2s. 6d.)

The handling of cotton in its early stages is a dusty occupation and is the cause of much respiratory disease among operatives. The author of this report shows that cotton dust contains a specific agent capable of producing the symptoms observed; this agent is contained in the protein fraction of the dust, and in persons who are specially sensitive it produces the disease, which is related to ordinary asthma. The remedy lies in the installation of improved machinery capable of preventing access of this dust to the respiratory tract.

No. 214. Catalogue of the National Collection of Type Cultures. Fourth Edition. (H.M. Stationery Office. 2s. 6d.)

Five years have elapsed since the publication of the third edition of this useful catalogue, during which time many species have been added. The nomenclature adopted is that recommended by the International Society for Microbiology, but having regard to the present somewhat

transitional position it has been found necessary in many cases to give also the name by which the organism has hitherto been known The generic term *Bacillus* has been restricted to spore bearing bacteria but the adoption of the term *Clostridium* for anaerobic spore bearing bacteria has been left over for future decision The catalogue should be of great service to microbiologists

MERCK'S JAHRESBERICHT for 1935 contains (in German) the usual very complete summary of the year's progress in therapeutics with two special articles on Vinethene (vinyl ether) as an anaesthetic and a number of notes on vitamins In the therapeutic summary the references to sex hormones are an outstanding feature The book is issued by E Merck Chemische Fabrik Darmstadt.

Literary Physicians of the Twentieth Century[1]

By R CECIL OWEN B Sc Lond, F C S etc

ARCHIBALD JOSEPH CRONIN is barely forty His literary career is being watched by critics and discerning readers with lively interest It is felt that he may come to be regarded as one of the major novelists of the period The uncertainty of his as of so many young writers, future lends a certain fascination to speculation To use a threadbare phrase he became famous overnight With the publication of his first novel *Hatter's Castle* (1931) he sprang into instant and universal fame It was a novel in the grand tradition—full of promise and a considerable achievement too Spread over a large canvas it dealt with the perennial passions vanities aspirations and conflicts Though marred by a violence and crudity natural enough in a first effort it was felt to be the work of a mind powerful and sincere of an imagination vivid and far-seeing Subsequent work might well include a masterpiece Unfortunately it has to be recorded that the later novels are definitely on a lower plane of achievement *Three Loves* came next in 1932 Although there is much in it that is pathetic and humorous and although the characters are on the whole well drawn there is a marked tendency to fall into bathos sentimentalism and false judgment especially towards the end of the book where the author seems to tire *Grand Canary* (1933) is a less ambitious work—a fine story told with humour and gusto full of sensational episodes and if nothing else very good entertainment *The Stars Look Down* (1935) is again a long ambitious novel written with a politico social purpose—and the purpose as always except in the hands of a first rate artist thwarts the art Many of its episodes are intensely moving but iteration tires the reader and a certain lack of restraint defeats the lesson it would teach If this brilliant novelist resists the temptation to be spoiled by success he may yet attain to the first rank

Dr Cronin would be classed as a successful and outstanding physician He took both M B and M D with Honours in the University of Glasgow and he holds the coveted prize of M R C P England as well as the D P H After practising in the West End of London for a dozen years he abandoned medicine entirely for literature To-day he is besides a novelist a journalist much sought after by the best paying periodicals His future is still obscure, we can but wait and see!

[1] Previous articles dealing with A. Conan Doyle W Somerset Maugham Robert Bridges and Francis Brett Young appeared in THE PRESCRIBER for June 1932 p 218 and Nov 1934 p 367

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COMMON MALADIES AND THEIR TREATMENT.

XXXVI. Minor Gynaecological Disorders.

By Dorothea M. Tudor, M.B., B.S.
Leamington Spa.

Among the minor gynaecological disorders may be classed those which are non-malignant, are not dangerous to life or requiring major operative treatment, and do not cause complete invalidism. If, however, the suffering, inconvenience, and incapacity which they entail, and the vast numbers of women affected are taken into account, this group of disorders deserves all that skill and perseverance can do to prevent occurrence and to relieve the distressing symptoms when they do arise.

Pruritus Vulvae is a condition in this category of morbidity which is as common, or more so, in the practice of the family physician as in that of the gynaecologist. The underlying causes are many and various, and its successful treatment is often exceedingly difficult, requiring experience and resourcefulness on the practitioner's part.

The symptom can manifest itself at any time of life, from a few days after birth to old age. In some cases the cause is quite apparent and the cure simple. In others the most careful examination does not reveal any local lesion to account for the irritation, or to indicate that such is present, except perhaps abrasions from scratching.

The possibility of irritation about the vulva should be remembered if infants are fretful and restless or subject to attacks of screaming which suggest temper or hysterical outbursts. Examination may reveal the presence of vulvitis due, even in well cared-for infants, to lack of cleanliness, through neglect to separate the labia and remove smegma and accumulated excreta when washing the child. Vaginal

discharge, not necessarily gonococcal, is another cause of infantile vulvitis. Irrigation of the vulva several times daily with weak boracic lotion through a sterilized catheter attached to a douche can, followed by drying of the parts with sterilized swabs, may be sufficient treatment. But occasionally it is necessary to follow the vulval irrigation with vaginal douching, when scrupulous aseptic precautions must be taken, and the lotion run in under very low pressure. Irrigation of the vulva must always precede and follow the vaginal wash-out. Whenever a vaginal discharge exists the baby should be laid in the prone position several times a day to promote drainage.

Lack of cleanliness is a common cause of pruritus in children and women. Patients seen in industrial practice seldom realize that the parts require washing with soap and water at least once a day. They become soiled by excreta or menstrual blood, and, in children especially, by dust and dirt, which give rise to soreness and itching.

A frequent source of irritation is the migration of threadworms from the anus to the vaginal orifice in dirty children whose perineum is soiled by excreta. The treatment is that for the eradication of the worms, combined with local cleanliness and precautions against reinfection from the ova collected in the crevices of the child's nails.

Eczema, herpes, and urticaria may all affect the genitalia. When prescribing for the general condition special measures are necessary for the relief of the local irritation.

In treating the pruritus from which diabetics are prone to suffer, the probability of infection, usually a mycosis, must not be forgotten (Lawson Tait). The local application of gentian violet (one per cent. aqueous solution) is reported to be most efficacious in eradicating the fungus.[1]

Kraurosis Vulvae may appear in early middle life, but it is usually about the menopause and later that it develops. It is probably due to constitutional degenerative changes of which the condition of the skin about the vulva and intense irritation are signs and symptoms. The skin of the external genitals and the perineum has a smooth glazed appearance, with heaped-up indurated areas. All the parts become very pale. There may be small subcutaneous haemorrhages, and tears and abrasions from scratching are always found, the itching being so intense as to be almost unbearable.

For treatment, the application of strong nitric acid to

1 Plass, E. D., Hesseltine, H. C., and Borts, I. H. Monilia valvovaginitis, *Amer. J. Obstet. & Gynec.*, 1931, Mar., 320-334; also Prescriber, 1931, Nov., 347.

the indurated patches gives very satisfactory results in many cases, improvement and alleviation of the itching often being noticed after the first application. The method is to dress a small probe with cotton-wool, dip it into strong nitric acid, and apply the tip of the probe to two or three of the hardened areas. Care must be taken to avoid bringing the acid into contact with normal skin or mucous membrane or any cracks or abrasions, otherwise severe burning will result. Not more than a few separate patches should be treated at each sitting, and water should be at hand so that if the acid leaks beyond the indurated surfaces it can be immediately washed off. This procedure is repeated about twice weekly, different plaques being treated each time, and in a few weeks complete relief from symptoms is generally obtained. If more convenient the thermo-cautery can be used instead of nitric acid.

In addition to local applications general treatment will be necessary. The nature of this will depend on the patient's constitutional condition, but thyroid medication is suggested.

In distinction to the obvious lesions of kraurosis there is the intense vulval itching, unaccompanied by any marked external change beyond the abrasions from scratching, which may lead to secondary infection and eczema. Study of its pathology, however, has shown changes in the deeper layers of the skin of the nature of a slowly progressing fibrosis which affects the nerves and nerve endings of the labia minora and clitoris. Relief may be obtained by the application of soothing ointments. Cold dressings, as with lead lotion, are successful in some cases; also sitz-baths of normal saline, or of an alkaline solution such as sodium carbonate. A bath recommended by Macnaughton Jones consists of bran 2 lb., potato starch ½ lb., gelatin 1 lb., water at 100-105° F. 25-30 gallons. If external applications fail the operation of dissecting up flaps of the affected skin and replacing them has proved satisfactory, the object being to sever the nerves from their skin endings.

Some women suffer single or recurrent attacks of irritation which cannot be attributed to any local pathological condition but coincide with periods of overwork, disturbed nights, anxiety, or worry. Removal, so far as is possible, of mental and physical strain is an important detail of treatment. A few days' rest in bed is desirable, with copious intake of fluids such as hot water, glucose, and very weak freshly-made tea. Change of air, from a relaxing climate to the sea or moors, will often banish the trouble in a few

hours. Locally soothing ointments or lotions are indicated, and several may have to be tried before the one suited to the particular patient is found. Hot water sitz-baths ease some women, others get more relief from icy cold bathing. Ichthammol (10 per cent. in glycerin) is often useful.

Vaginal Discharge.—Any patient complaining of discharge from the vagina must be induced to consent to a local examination. Whatever the age of the woman or girl the possibility of gonorrhoea will not be forgotten.

Simple leucorrhoea may be due to the habit of douching, and will clear up when this is broken. When it is a symptom of some systemic condition the treatment is for that underlying cause. In case of a discharge being very profuse, offensive, or purulent, the vagina, after the vulva has been swabbed, should be washed with cotton-wool held in long-handled forceps and saturated with solution of sodium bicarbonate. When the cervix and vagina are clear of discharge the parts should be dried with wool, and then a strip of gauze moistened with lactic acid (2 per cent.) or a lactic acid pessary should be inserted. The patient can remove the gauze tampon herself in twenty-four or thirty-six hours. The use of a fenestrated speculum facilitates thorough swabbing of the vaginal walls.

Cervical Polypi may cause muco-purulent discharge, haemorrhage, slight or severe, or no symptoms. Treatment is unnecessary so long as symptoms do not supervene. But the possibility of the growth increasing in size must not be lost sight of, and the patient should be cautioned to seek advice if it gives trouble.

When discharge exists operation is advisable, and with haemorrhage bleeding is often so severe as to make removal essential. The operation of catching the polypus in a volcellum and twisting it off is usually all that is required, but it must be done under general anaesthesia.

Urethral Caruncle is another growth which can safely be left alone so long as it does not cause inconvenience, but the painful form must be removed. The operation is easily done under local analgesia.

Cystocele and *Rectocele* are best treated in their early stages by plastic operation. A pessary is often fairly satisfactory in younger women, but as age advances and the parts become lax it frequently cannot be retained, or the development of cervical erosion will necessitate its being discarded. Then operation may be impossible and the patient has to endure the misery of genital prolapse.

EYE DISEASES: RECENT WORK.

THE use of gold sodium thiosulphate in certain ocular conditions is discussed by KOENIG (Buffalo), who has tried gold therapy in cases that might be suspected to be of tuberculous origin but in which the aetiological factor could not be discovered The first case was one with a history of gradual blurring of vision in both eyes The corneae were clear and no external abnormality could be observed, but the vitreous presented a dense haze of flocculent opacities The visual acuity was 6/60 in each eye Weekly intravenous injections of 10 mg of gold sodium thiosulphate effected improvement in vision Fifteen such injections were given with gradually increasing doses, and after a month's rest these were resumed and continued as long as improvement could be observed After a year the visual acuity had increased to 6/9 corrected to 6/6 Other cases of dense vitreous haze some exudative and others haemorrhagic, were similarly treated but only after other treatment and elimination of foci of infection had failed to effect any improvement Several cases of severe iridocyclitis were treated after the acute symptoms had subsided and a vitreous haze remained causing a diminution in visual acuity The routine treatment was to start with a dose of 10 mg , increasing this to 25 mg for six weekly doses in order to detect any sensitivity to the drug After that the dose was increased to 50 mg until fifteen doses had been given A month's rest was then allowed, after which the 50 mg dose was resumed for another fifteen injections If no improvement was noted by that time it was concluded that none would result

According to GUNDERSON, *the deposits of iron seen at the site* of a subconjunctival injection of adrenaline are due to the dissolution of the iron of the needle by the hydrochloric acid of the solution as well as to the reducing action of the adrenaline The use of chrome steel needles will minimize this trouble, but it is better to use needles of gold or platinum The adrenaline solution should come in contact with the needle for as short a time as possible Pledgets soaked in adrenaline solution and kept under the lid for a few minutes have practically the same mydriatic effect as injections

Allergic Conjunctivitis —LAGRANGE (Paris) discusses spring catarrh and allied conditions characterized by perilimbic gelatinous infiltrations and pavement like proliferations occurring in the tarsal conjunctiva Its nature consists of pruriginous cutaneous or mucous reactions They appear and cease abruptly, thus assuming the character of crises, and are associated with other anaphylactic signs, such as endocrine syndromes, developmental disturbances, or disorders of puberty or the menopause Bacteriological examinations are negative and smears show no including cells but a certain number of eosinophilic cells Cutaneous or intradermal reactions are positive, and so is the Prausnitz Kutzner *test for passive allergy* Adrenaline and ephedrine act immediately and temporarily Cessation of

A bigger hole is then made in the sclera to remove the subretinal fluid The retina is thus allowed to fall back into position After treatment consists in the instillation of atropine and mild silver proteinate (argyrol) Oedema of the lids and chemosis are usually present and the patient is kept quietly in bed Cases with complicated cataract give uniformly bad results Another bad prognostic sign is long duration of detachment with fixation of the retinal folds The type of detachment resembling a distended firm balloon also responds badly to treatment

[An article on Detachment of the Retina in which various methods of treatment were reviewed appeared in THE PRESCRIBER for November 1935 pp 341 344]

Embolism of the Retinal Artery —ORR and YOUNG (Wolverhampton) report a case of retinal embolism in which subconjunctival injections of acetylcholine (one per cent solution) were used with good results They injected 4 minims on the lower temporal quadrant and 4 minims in the lower nasal quadrant as far back as the equator of the globe The first injection was relatively painless but the second was slightly painful for about five minutes The retinal exudate was absorbed within 3½ hours The conjunctival oedema following the first injection subsided within 14 hours but that following the second injection lasted 30 hours No corresponding dilatation could be observed in the vessels of the other eye

Retinitis —SIMPSON (Bristol) reports a case of retinitis successfully treated by protein shock The patient a man aged 70 had found his vision failing for some months but with no pain or photophobia Visual acuity of each eye was 6/60 No external defect was visible and the pupils reacted normally but the fundi showed congestion round each disk extending to the macula around which were numerous small dots of exudate Search was made for septic foci and several teeth were extracted Potassium iodide (5 grains thrice daily) was given A fortnight later as no improvement could be observed a series of three intravenous injections of anti typhoid paratyphoid (T.A B) vaccine was given in doses of 10 25 and 50 millions at intervals of two days Marked improvement followed the congestion disappeared and after a few months *the visual acuity was 6/6 (left) and 6/9 (right) with glasses* A year later the improvement was still maintained

Tobacco Amblyopia —In this condition the defect is said to be due to constriction of the macular arterioles and paralysis of the synapses in the cone fibres or of the bipolars The degenerative changes in the ganglion cells may be secondary to the vasoconstrictive effect of nicotine Formerly it was held that the pathological process in the papillo macular bundle was an interstitial sclerosing inflammation with secondary nerve atrophy, and it was customary to treat the condition with iodides and strychnine More recent observers inclining to the opinion that vasoconstriction from

nicotine poisoning was the primary cause, have based their therapeutic measures accordingly. Sodium nitrite has been used in many cases in doses of 0·04 gm. on each of the first three days and 0·1 gm. afterwards.

Another drug which has recently been used with some success is acetylcholine. ORR (Wolverhampton) reports four cases in which acetylcholine was given with most satisfactory results. Three of the cases were chronic and furnished a severe test for any therapeutic agent: the fourth was acute and the treatment was equally successful. The drug was given intramuscularly in doses of 0·1 gm. daily or every other day for a period of six to ten days.

P. A. H.

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EAR, NOSE, AND THROAT: RECENT WORK.

Ionization in Ear and Nose Conditions.—In certain diseases of the ear, ionization may be looked upon as a well-established procedure, giving good results in a large percentage of cases. The usual routine consists of the application of antiseptic drops locally, with astringents, accompanied by vaccine treatment in certain cases. The contraindications of ionization are chronic cases with mastoid infection, aural polypi, and cases with ascending infection of the eustachian tube. Success depends on thorough cleansing of the ear, and bears a distinct relation to the degree of severity. Cases with slight discharge and little inflammation may require only a single treatment. The method is economical and free from risk.

of any focus of disease in the nose and naso-pharynx, it is necessary to treat any latent mastoiditis, chiefly in young children If an acute otitis media does not resolve in from ten to fourteen days, and if radiograms point to mastoid infection, then an operation is performed Every attempt is made to preserve the hearing power This can be promised if the infection is confined to the atrium of the middle ear and the perforation is central Treatment consists of the application of hydrogen peroxide followed by careful syringing with boric acid lotion, after this he uses drops of rectified spirit or powdered boric acid with one per cent iodine If there is no sign of improvement in these cases after two or three months in adults and one or two months in children, he resorts to surgical interference Minor surgery to promote better drainage and better penetration of the medicaments consists in the removal of diseased tissue and other conservative methods The radical operation, however, is called for in the presence of intracranial complications, acute exacerbations with facial paralysis, cholesteatomatous involvement, sagging of the posterior meatal wall, evidences of underlying osteitis, or in the case of failure of conservative treatment

Writing on the subject of prognosis in otorrhoea, HOWARTH mentions that the condition is common in all age periods, producing discomfort and suffering and often associated with serious disabilities The disease is anything but trivial and requires methodical treatment In the majority of cases the infection goes through the eustachian tube, although in sucklings it may be blood borne It follows colds, influenza, specific fevers, and unhealthy conditions of the nose and naso pharynx, such as adenoids Swimming bath infection is a common cause of otorrhoea In infants the eustachian tube is short, wide, and straight, and lined with a mucous membrane that is prone to infection Infants with colds and nose and throat infections should be isolated The onset of infection is accompanied by blocking of the eustachian tube opening into the middle ear while the attic is shut off by swelling of the mucomembranous folds of Troltsch The symptoms are earache, fever, sleeplessness, and general malaise When the infection is virulent, or in the case of old people and those lacking in resistance, the otorrhoea does not clear up after paracentesis, everything must be done to facilitate drainage from the tympanic cavity, a gauze wick should be carried down to the hole in the drum and changed at frequent intervals, with gentle syringing or mopping of the discharge and the insufflation of a dry powder such as one per cent iodine in boric acid The prognosis for hearing is good except in cases where the drum does not heal If the discharge lasts more than three weeks the inflammation has spread to the attic and mastoid antrum, and operative interference may be necessary

Discussing streptococcal infections of the middle ear, MOLLISON (London) remarks that the commonest cause is an acute infection of the whole upper respiratory tract, such as the common cold, influenza, tonsillitis, etc Should the antrum become infected,

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ear infection is more likely. When measles and scarlet fever are the cause of the mucous-membrane infection the ear is very often involved, while bathing in fresh-water baths is a common cause. Referring to treatment, he describes a case in which streptococcus antitoxin (scarlet fever) was given with advantage prior to mastoid operation; in another blood transfusion effected recovery without operation. Injections of pentnucleotide mark a great advance in the treatment of severe cases, and Mollison thinks that these alone might raise the patient's resistance to such an extent as to avoid the transfusion.

Dealing with the conservative treatment of middle-ear suppuration, CLEMINSON (London) remarks that the primary considerations are: (1) to prevent the original infection due to a single organism (usually a streptococcus) from becoming a multiple infection; (2) to keep the meatus clean and to prevent accumulation of discharge; (3) watchful care in looking out for complications. Syringing is preferable to mopping when the discharge is abundant. Instillation of solution of hydrogen peroxide will make it easier to dislodge a sticky discharge, while a solution of boric acid is a satisfactory lotion for syringing the ear. When the pus is mucoid in character sodium bicarbonate should be added in quantity equal to the boric acid. Mercurochrome (0·5 per cent. aqueous solution) used as drops has been found to clear up cases that have resisted other treatment.

BETTINGTON (Australia) reports on the popular method of treating otorrhoea by insufflation of boric acid powder containing 0·75 per cent. of iodine. The meatus must first be cleared of discharge by mopping, sucking, or careful syringing, and the ear dried with swabs and puffs of dry air. The powder must be kept in a stoppered bottle and renewed at least once a fortnight as dissociation is very rapid. All types of running ears, except those with furuncle, can be treated with this powder. Some patients complain of severe pain for a short time after its application, and occasionally the iodine can be tasted for about half an hour. Bettington has had good results also in external and acute otitis, and he is of the opinion that the treatment will dry up the discharge more rapidly than any other method.

The operative treatment of chronic suppurative otitis media is discussed by SHERIDAN (Liverpool). The mastoid operations are performed with the threefold purpose of removing dangerous disease, preserving hearing, and healing the ear. His observations show that many mastoid incisions are too short and badly curved, the bony meatus is too narrow for correct supervision, the antrum remains as a recess, and the bridge is too timidly removed, the result being that a prominent facial ridge is left and a eustachian fistula exists. These causes of failure can be avoided by prolonging the incision to the anterior part of the tip of the mastoid. The mastoid bone should be hollowed out extensively and the whole of the posterior meatal wall removed. Shavings of bone are removed from below upwards, so that were the facial canal opened the nerve would

be recognized Exposure of the lateral sinus and dura is of small consequence provided the dura is undamaged Light curettage of the tympanic annulus is necessary to get rid of any osteitis A second series of cases is described which were subjected to paracentesis after the discharge had commenced, on account of pain, tenderness over the mastoid, and elevation of temperature Frequently on incising the drum in these cases pus escapes under pressure, and on account of the virulence of the infection and the poor resistance of the patient nearly 20 per cent require the simple mastoid operation After the operation is completed saline is syringed by way of the aditus through the perforation into the external auditory meatus The cavity is filled with absolute alcohol, dried and packed with narrow iodoform gauze, and the external meatus is plugged to prevent narrowing of the canal Sheridan strongly advocates early paracentesis to prevent acute mastoiditis, only 7 per cent of patients who have had an early paracentesis require a mastoid operation

Otitis media as a complication of scarlet fever still presents many problems Several of these were discussed by McGregor and others at a recent meeting of the Society of Medical Officers of Health Emphasis was laid on the importance of careful treatment of acute cases of scarlet fever Notwithstanding the fact that this infection is milder than formerly and that serum is frequently given, the percentage of otitis media is much the same Ten per cent of deaf mutes and the same number of otitis cases are due to scarlet fever Children under five show the heaviest incidence Suppuration does not always take place More often than not there is a low grade inflammation, subsiding slowly after several weeks The drum membrane should be examined frequently, daily if possible, *and always on discharge from the fever hospital During the first* week or two the discharge shows a pure culture of the haemolytic streptococcus later secondary infection with skin organisms occurs The prognosis of scarlatinal otitis media is better where serum has been injected after intramuscular injection it varies between 3 5 and 8 4 per cent, after intravenous administration the incidence is around one per cent Respiratory complications, nasal diphtheria, measles, whooping cough, and tonsillitis have a bad effect on the prognosis The most important principle in treatment consists of rigid meatal antisepsis by the frequent use of sterile wool mops

Nasal Sinus Disease —Inflammation of the air cells in and *around the nose is of wider occurrence and of greater importance* than is generally suspected Tilley (London) shows how the sinuses are developed by extensions from the nasal cavities into the cancellous tissue of the adjacent maxillary ethmoid, frontal, and sphenoid bones Almost limitless variations of the normal topographical relations of the accessory sinuses are possible Apart from mere anatomical contiguity an important point is the vital connexion between the air-cells and the parent nasal cavity by means of a continuous mucous

membrane. This membrane is composed of ciliated epithelium and secreting goblet cells on a fibro-elastic stroma in which many types of defensive cells are scattered. The mucosal defence consists of mucus which enmeshes dust, organisms, etc., the cilia, which wafts the mucus onwards, and secretions from the glandular nodes in the stroma. It has been shown that lymphatic infection may spread from the antrum into the mediastinum along the lymph vessels. More commonly infection spreads by surface continuity and by vascular channels. Tilley also draws attention to the possibility of spread from an apical abscess and from extensive pyorrhoea of a tooth socket. When symptoms of inflammation develop in or around an upper bicuspid or molar tooth, treatment should immediately be instituted to prevent antral infection and destruction of cancellous alveolar bone. In the ordinary non-dental infection congestion and oedema in the antrum prevent free drainage.

Streptococcal Throat Infections.—Acute streptococcal infection of the pharynx and larynx has been recognized as a number of different conditions. DAVIS (London) remarks that the great variation in the clinical signs and symptoms depends upon the severity and type of the infection, the resistance of the patient, and the situation of the lesion. For clinical purposes he recognizes two chief degrees of inflammation: tonsillitis, with variation in severity and extension to surrounding tissues, and a gangrenous inflammation, with a sloughing membranous exudate and toxaemic and septicaemic symptoms often beginning with acute tonsillitis. Such infections are serious and demand careful treatment; active co-operation of the bacteriologist, surgeon, and physician is necessary. If there is any question of diphtheria, serum should be given at once. In streptococcal infections large doses of streptococcus antitoxin (scarlet fever) are called for. Complications are numerous, and the throat condition may be part of a general infection. P. A. H.

Mollison W M Acute streptococcal infections of the middle ear *B.M.J.*, 1936 Sept 26, 615 617
Sheridan M R Chronic suppurative otitis media its operative treatment *B.M.J.* 1936 Apr 18 791 792
Tilley, H Chronic pyogenic inflammation of the maxillary antrum and other nasal accessory sinuses (Semon Lecture) *Med Press* 1935 Feb 13 148 155, Feb 20, 173-182

THERAPEUTIC ABSTRACTS.

Sodium Citrate as a Spirochaeticide.—Leadingham (Atlanta, Ga) reports the accidental discovery that a drop of 2 per cent sodium citrate solution on a slide containing the spirochaetes of Vincent's angina caused the organisms to cease movement with apparent eventual dissolution Repeated experiments gave the same result Later, the same solution was applied to the ulcer from which the specimen had been taken, and in ten minutes no organisms were found They did not reappear on subsequent days and the patient was dismissed It is suggested that the drug might find a place in the treatment of spirochaetal infections

Leadingham R S Sodium citrate—a spirocheticide *J Lab & Clin Med*, 1936, June 922

Prostigmin and Curarine—Briscoe (London) has studied separately the peripheral actions of prostigmin and curarine, and shows that both are capable of producing acute depressant effects, which, however, are not identical Their mutual antagonism is such that normal muscular action can be preserved when poisonous doses of the drugs are exhibited together These results are explained on the hypothesis of chemical transmission of excitation, and it is shown that they have application to the problem of myasthenia

Briscoe G The antagonism between curarine and prostigmin and its relation to the myasthenia problem *Lancet* 1936 Feb 29 469 472

Fouadin in Undulant Fever—Neumann (Malta) reports treatment of eight cases of undulant fever with fouadin, a compound of antimony with a derivative of pyrocatechin (Bayer) All the patients made good recoveries The drug was injected intramuscularly in doses of 1 5 c cm on the first day, 3 5 c cm the second day, and thereafter 5 0 c cm (females 4 5 c cm) on alternate days The drug was well tolerated and no secondary effects were observed Tanner (Newton Abbot) also records a case similarly treated The same dosage was employed and the result was very satisfactory

Neumann, C Z On the treatment of undulant fever with fouadin *Lancet*, 1936 May 2 1001 1002
Tanner G M Undulant fever treated with fouadin. *Lancet*, 1936 Sept 19 684 685

Aetiology of Peptic Ulcer.—Discussing the various factors believed to be responsible for the formation of peptic ulcer, Littwich (Johannesburg) concludes that probably no one factor is responsible The mucous membrane of the stomach, he says, is a battle-ground

on which there is attack and defence between factors that will cause ulcer and those that will heal it. No doubt in all stomachs small abrasions due to trauma by food appear, healing without difficulty in the majority of cases. In others, these small abrasions are eroded further by the acid gastric juice and are allowed no opportunity to heal. Some change in the reaction of the acid, due possibly to climatic variation or improvement in mental stability, results in a remission of symptoms and partial or complete healing of the ulcer.

LEFTWICH, P. The aetiology of peptic ulcer *South African Med. J.*, 1936, June 27, 436-439

Pharmacology of Ergometrine.—As the result of a study of the pharmacology of ergometrine, GHOSH, DATTA, and ADYA (Calcutta) arrive at the following conclusions: (1) Ergometrine has very little effect on the non-gravid uterus. (2) It causes powerful contractions of the gravid uterus, making these stronger and regular, and it does not throw the uterus into tetanus. (3) It stimulates the heart directly, making the beats stronger and quicker. (4) It causes a slight rise of blood-pressure, which though not very high is distinct. (5) There being no peripheral vasoconstriction it has no gangrene-producing effect like ergotoxine.

GHOSH, B N, DATTA, C C, and ADYA, P C A preliminary observation on the pharmacology of ergometrine *J. Indian Med Assoc*, 1936, June, 519-520

Test for Latent Jaundice.—The following test for latent jaundice is recommended by BRODRIBB and CULLINAN (London) as being applicable to cases of cholelithiasis, catarrhal jaundice, pernicious anaemia, etc. The patient is placed in good daylight (artificial light is unsatisfactory) and a small area of skin is cleansed with spirit. One minim of a sterile solution containing 0·1 mg. of histamine is injected *intradermally* into this area. In about five minutes a circular weal, surrounded by an erythematous zone, develops at the site of injection and reaches its maximum in from ten to twenty minutes. If the result is positive the weal is definitely yellow when compared with the adjoining normal skin. If there is any doubt about the yellow colour the reaction is regarded as negative.

BRODRIBB, H. S, and CULLINAN, E R A simple test for latent jaundice. *Lancet*, 1936, May 30, 1237-1238.

Drugs and Idiosyncrasy.—According to WITTS (London), the toxic effects on the blood-forming organs of drugs such as amido-pyrine, neoarsphenamine, and gold are usually the result of idio-syncrasy and occur with doses that are well within the ordinary therapeutic limits. In certain cases the patient becomes sensitized to the drug and an allergic type of response occurs. Considerable hardship may result from failure to realize the small dosage which may be responsible for damage to the bone-marrow in predisposed individuals, the long incubation period, and the protracted duration of the lesion.

WITTS, L. J. Effect of toxic substances on the blood-forming organs, with special reference to therapeutic drugs. *B M J.*, 1936, Aug 1, 211-215.

THERAPEUTIC NOTES.

Proteinuria.—G A HARRISON (London) suggests the term 'proteinuria' as being more accurate than 'albuminuria' which is generally employed The tests for this condition are not exclusively indicative of albumin but reveal the presence of urinary proteins as a group —*Med Press*, Sept 2, '36, p 189

Tetany following Adrenaline.—ELLSWORTH and SHERMAN (Baltimore) record a case in which tetany followed the administration of adrenaline for relief of asthma Blood calcium was normal and the tetany appeared to be due to alkalosis resulting from hyperventilation —*J A M A*, Jan 25, '36, p 284

Haemophilia Placental Extract—ELEY, GREEN, and MCKHANN (Boston) report that human placental extract (placimmunin, see PRESCRIBER, May '36, p 200) has proved very effective in treatment of haemophilia It is given orally or intramuscularly, but must not be given intravenously —*J Pediat*, Feb '36, p 135

Haemophilia Snake Venom—BAKER and GIBSON (Torquay) report a case of very severe bleeding after tooth extraction—it had lasted for ten days and the patient was exsanguinated—which was at once stopped by the application to the tooth socket of a dilution of Russell viper venom —*Lancet* Feb 22, '36, p 428

Measles Convalescent Serum—G W ELKINGTON (Malvern) describes an epidemic of measles occurring in a school Attenuation was obtained in 21 cases by 5 c cm of convalescent serum, an entire absence of cough and toxaemia resulting In the non protected cases appendicitis and albuminuria occurred as complications — *B M J*, Feb 15, '36, p 308

Cholera. New Serum—H GHOSH (Calcutta) reports further on his serum for cholera (see PRESCRIBER, Nov '35, p 358) Intraperitoneal administration has a specific therapeutic effect, and the uniformly good results leave no doubt that its use will greatly diminish the mortality —*B M J*, May 9 '36, p 936

Cholera Acidosis Sodium Lactate—BANERJEE and DATTA recommend the intravenous use of sodium lactate in place of bicarbonate in the treatment of cholera acidosis The lactate ion is transformed into glucose and the sodium ion so liberated combines with the excess of CO_2 to form a rapid supply of bicarbonate Alkalosis is thus avoided —*J Indian Med Assoc*, 1936, Jan, 168 169

Cataract: Ascorbic Acid.—E M JOSEPHSON has used ascorbic acid in all forms of cataract While the results in senile cataract were gratifying, those in dinitrophenol cataract are described as surprisingly rapid —*Science*, 1935, lxxxii 222, per *B M J*, Oct 19, '35, p 731

REVIEWS OF BOOKS.

A Manual of Pharmacology By the late Walter E Dixon, revised by W A M Smart, M B, B S, B Sc Eighth Edition Pp 483 (Edward Arnold 18s)

Since the appearance of the seventh edition of this book the lamented death of its author has necessitated its revision by other hands Mr Smart has found it necessary to recast the work very thoroughly, by reason, as he tells us in his preface, of the rapid development of pharmacological research in all directions Revision has certainly been very thorough—so thorough indeed that the present edition is virtually a new book We do not say that it is not a better book, but it has to a great extent lost the stamp of the author's personality so characteristic of Dixon's work and has now become a general textbook on pharmacology

Apart from the rearrangement of the matter, the most noticeable feature of this edition is the prominence given to organic chemistry By means of graphic formulae the structure and inter-relationships of the various organic compounds are made clear and the bearing of molecular structure on therapeutic action is demonstrated A number of prescriptions have been introduced—some in Latin (not always correct), some in English, and some in a mixture of both These should be carefully revised before another edition appears, as must also some of the pharmacopoeial preparations on pages 28 to 32 It is rather vague to define glycosides (page 24) as 'combinations of the sugars with other substances'—a glycoside is a compound which yields a sugar (among other products) on hydrolysis, which is not quite the same thing 'Basal narcosis' is now generally regarded as preferable to 'basal anaesthesia' (page 63) and Gwathmey's name has been wrongly transcribed on the same page These are only a few minor points, and they are offered as a help to the author in preparing his next edition, which will surely be called for soon The work well maintains its place as a standard textbook T S

A Treatise on Materia Medica and Therapeutics By the late Rakhaldas Ghosh Fourteenth Edition, by B N Ghosh, F R F P & S Glas Pp xv+724 (Hilton, Calcutta H K Lewis, London 12s 6d)

A work which has reached its fourteenth edition in thirty five years calls for little comment from a reviewer The present edition has undergone very thorough revision not only has it been brought into line with the British Pharmacopoeia, but many of the newer and as yet unofficial remedies have been included A feature of the work is its application to Indian requirements, not only in regard to the drugs included but also with reference to their therapeutic action in the treatment of tropical diseases The book is well printed on good paper, the illustrations are few, but they are well chosen and helpful to the text, the index is well arranged and inclusive The book is to be commended to students and practitioners, especially those working in the East T S

The British Pharmacopoeia Commission of the General Medical Council has issued a Report by the Sub Committee on the ACCURACY OF BIOLOGICAL ASSAYS (44 Hallam Street, London, W 1, 1s 6d) In this the various biological tests for drugs and therapeutic substances are reviewed, their accuracy and limits of error are discussed, and recommendations are made regarding their inclusion in the forthcoming

Addendum to the British Pharmacopoeia which, by the way, is promised for publication on December 29 1936

In a Report issued by the Board of Control, I G H Wilson M D, presents A STUDY OF THE HYPOGLYCAEMIC SHOCK TREATMENT IN SCHIZOPHRENIA (H M Stationery Office, 1s 3d) Dr Wilson has visited a number of clinics abroad where the method is in use and where the results are said to be very promising Insulin is injected intramuscularly in doses of 15 to 30 units, gradually increased, and this is continued until the patient falls into a state of hypoglycaemic shock after which the treatment is continued in a modified form until recovery is established Full details of the treatment are given, with illustrative cases and a series of recommendations for its trial in this country are appended

Years ago Dr Brett Young hit upon a useful formula (or prescription ?) and gave us *Portrait of Clare* The formula has been in operation ever since and TAR FOREST (Heinemann 8s 6d) is the latest proof of its efficacy As an entertainer Dr Young wins top marks but the serious student of letters demands something less like a box of confectionery—something more life like more astringent This is a book of 550 pages—twice the length of an ordinary novel—and too lengthy to sustain its rather slight plot Dr Young could produce a masterpiece if only he could learn to cut The scene is set in our author s favourite district, round Shropshire and Worcestershire and the story makes exciting reading but the background looms larger than the actual characters Mining districts and rural scenes are vividly depicted and the contrast is in the best artistic tradition The whole narrative is written gracefully and with care, we may overlook an occasional slipshod expression. One still hopes that Brett Young will write the great short novel of real significance of which he is unquestionably capable

Several interest ng Reports relating to the health of industrial workers have recently been issued The ANNUAL REPORT OF THE CHIEF INSPECTOR OF FACTORIES AND WORKSHOPS for 1935 shows an increase of accidents of 9 per cent. over 1934 and 32 per cent over 1933 due for the most part to the increased activity in industry The sixteenth ANNUAL REPORT OF THE INDUSTRIAL HEALTH RESEARCH BOARD shows satisfactory results in the endeavour to promote health and efficiency in industry An equally active organization is the NATIONAL OPHTHALMIC TREATMENT BOARD which has issued a Report on the results of an investigation into the question of sight examination in industry The investigation has been on a large scale and includes workers in many different undertakings The Report contains a plea for systematic eye examinat on at regular intervals and reveals the need for a scientific investigation to determine the value to industry generally of proper and systematic medical care of the sight of operatives

The amalgamation is announced of the two well known firms Endocrines Ltd and E H Spicer & Co Ltd Under the name of Endocrines Spicer Ltd the new firm carries on business at Watford Hertfordshire manufacturing edwenil acidophilus emulsion and the numerous endocrine and biochemical products for which these firms have h therto been responsible The new firm has issued a handbook of their specialties with full particulars of therapeutic application dosage and price a copy of which will be sent to any reader of THE PRESCRIBER on applicat on

The Abbott Laboratories have issued a useful brochure on NEMBUTAL the new hypnot c and basal narcotic manufactured by them The booklet describes fully the nature properties doses and administrat on of that useful drug Cop es can be obtained from the firm s representative Mr Park E Green 52A W gmore Street London W 1

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THE PHARMACOPOEIA ADDENDUM.

FOUR years have elapsed since the publication of the *British Pharmacopoeia* in 1932, years which have seen many advances in therapeutics The work has to a certain extent gone out of date, partial revision has become necessary and an Addendum has been prepared containing many amendments and not a few additions This book will be published on December 29, on which date it will become official Meanwhile advance copies have been distributed to the press, including this journal, for purposes of review Before any review can be published, however, we are called on to sign a document undertaking not to use the copy for any improper purpose, not to publish substantial extracts or anything that will interfere with the sale of the book, and not to sell or otherwise dispose of the copy ! Surely there is such a thing as honour among reviewers and editors, though official bodies do not seem to be aware of its existence Four years ago the General Medical Council promised to seek amendment of the law so that the work might not become official until some time after publication, but this promise is still a promise

The Addendum contains twenty-nine new monographs, as under —

Acetarsol (stovarsol ')
Acidum Ascorbicum
Antitoxinum Oedematiens
A Staphylococcicum
A Vibriosepticum
Argentoproteinum (' protargol ')
Bismuthi et Sodii Tartras
Bismuthi Oxychloridum
Calciferol (vitamin D)
Liquor Calciferolis
Liquor Iodi Aquosus
Mersalylum (salyrgan ')
Oleum Iodisatum (lipiodol ')
Pulvis Vitamini B_1
Calcii Chloridum Hydratum
Calcii Gluconas
Chiniofonum (yatren ')
Ergometrina
Ext Stramonii Liq *and* Sicc
Ferri Subchloridum Citratum
Histaminae Phosphas Acidus
Injectio Bismuthi Oxychloridi
Injectio Mersalyli
Serum Antipneumococcicum I and II
Sodii Thiosulphas
Theophyllina
Tryparsamidum

One monograph has been cancelled and numerous amendments have been made in the B P text

It is stated in the introduction that proprietary monopolies or restrictions have prevented the inclusion of certain drugs which might otherwise have found a place in the list of additions. The cancelled monograph is Liquor Ergosterolis Irradiati, which is supplanted by Liquor Calciferolis. The amendments to the B.P. monographs are mostly technical in character. The monograph on Acriflavine has been rewritten to bring it into line with present chemical knowledge. The new monographs have most interest for the practitioner as they include many drugs that have been in general use since 1932 and are now to have official recognition. Ascorbic acid or vitamin C may be obtained from vegetable sources or prepared synthetically. Calciferol is the recognized equivalent of vitamin D. An adsorbate of vitamin B_1 is known by the rather clumsy name of Pulvis Vitamini B_1: it has already been known as 'antineurin,' and the Pharmacopoeia might well have adopted some such term. Hydrated calcium chloride is more suitable for injection than the ordinary salt. Chiniofon is now a recognized remedy for amoebic dysentery. Ergometrine is the new alkaloid of ergot, now known to represent the activity of the liquid extract. Citrated ferrous chloride is a stable salt for the treatment of hypochromic anaemia; its dose is 3 to 5 grains. Histamine acid phosphate must not be mistaken for histidine, the remedy for gastric ulcer; it is used to stimulate the secretion of hydrochloric acid in the fractional test-meal. Mersalyl is a mercurial diuretic; it is administered in the form of an injection containing theophylline. Aqueous solution of iodine (Lugol's solution) contains 5 per cent. of iodine and 10 per cent. of potassium iodide. Iodized oil is used for diagnostic purposes. Theophylline and tryparsamide are already well known. Diphtheria prophylactic now includes alum-precipitated toxoid.

The Addendum for 1936 is a book of 132 pages and is printed and bound in style similar to the present Pharmacopoeia. Its price will be five shillings, and as already mentioned it will be on sale from 29th December, on which date it will become official. The book represents very thorough and painstaking work, and its compilers are to be congratulated on its completeness. In giving official recognition to remedies already established in practice it confers a distinct boon on the general practitioner.

DIABETES MELLITUS: RECENT WORK.

An Abstract Review.

IN a general article dealing with recent progress in severe diabetes, WHITE (Boston) remarks that the past five years have completely changed our conception of the aetiology, physiology, and therapy of this disease. New complications have been revealed, a new race of long-duration young diabetics has arisen, and even the eventual prognosis of the disease has been changed. Recent work suggests, but does not prove, its hereditary nature. Insulin therapy is in a transitional stage: the new protamine insulinate promises to revolutionize therapy and the severe diabetic will profit most. While some hope lies in the isolation of a pancreatropic hormone, which will prove a more physiological method of treatment than insulin, so far insulin and the protamine compound have been the great therapeutic advances.

HIMSWORTH (London), whose previous work in this direction has already been mentioned in these reviews, now shows that two different types of disease can be distinguished as causing the symptom-complex of diabetes mellitus. One, the insulin-sensitive type, appears to be caused by deficiency of insulin; the other, the insulin-insensitive type, is apparently due not to lack of insulin, but to lack of an unknown factor which sensitizes the body to insulin. He describes a test for distinguishing these two types, and points out that the appropriate dietetic treatment of the two diseases may differ.

Discussing the question of trauma as a factor in the production of diabetes, HERBST (Kiel) concludes that trauma may determine the appearance of diabetic symptoms in a predisposed person with congenital weakness of the islet tissue who would in any case sooner or later have suffered from the disease, but that trauma cannot initiate the disease in a healthy individual.

The known relationship between the anterior pituitary and the pancreas has suggested the possibility that the pituitary is concerned in the production of diabetes. This question was fully discussed in our recent Endocrinology Number (PRESCRIBER, 1936, May, 182-183), where it was shown that among the numerous factors secreted by the anterior pituitary, three had been recognized as having an influence on the pancreas—a diabetogenic factor concerned with carbohydrate metabolism, a ketogenic factor influencing fat metabolism, and a pancreatropic factor controlling the secretion of insulin by the islets of Langerhans. In 1931 Houssay (Buenos Aires) showed that the anterior pituitary contains a principle antagonistic to insulin, and other workers have since shown that the same gland has a direct influence on the islets of Langerhans. Animals from which the pituitary has been removed become very sensitive to the action of

tuberculosis and diabetes is not known it seems reasonable these workers think, to believe that diabetes changes the tissue resistance making it more favourable for the development of tuberculosis Once tuberculosis has reached an advanced stage even when the diabetes is controlled the prognosis is poor It is therefore important to have early and frequent x ray examinations of the chest of all diabetic patients in order to detect and treat pulmonary lesions at the earliest stage

Sea-Sickness —HOST (Norway) shows the danger of sea sickness when it overtakes diabetic patients treated by insulin He cites the case of a young woman who had achieved a satisfactory equilibrium on insulin and suitable carbohydrate diet On a short sea trip she became sick eating little but taking her customary amount of insulin For some days after she landed the nausea persisted vomiting and diarrhoea ensued and coma set in Health was restored by means of large doses of insulin The coma was evidently precipitated by upset of the insulin balance when at sea

Coronary Thrombosis —The clinical association of diabetes mellitus and coronary disease has long been recognized RAAB and RABINOWITZ (Brooklyn) report cases to show that glycosuria and hyperglycaemia frequently occur during the acute stage of coronary thrombosis not preceded by diabetes In order to determine the influence of latent diabetes on this glycosuria and hyperglycaemia sugar tolerance tests were made in a series of non diabetic cases of coronary thrombosis All the recent cases gave an abnormal response while the majority of the older cases gave normal curves It is concluded that the glycosuria and hyperglycaemia of the acute stage of coronary thrombosis is not dependent on a latent diabetes Disturbance in the negative centres of the brain is offered as an explanation

The use of insulin in diabetes complicated with coronary sclerosis in elderly patients has been studied by COLLENS STOLIARSKY and NETZER (Brooklyn) They find it to have a remarkable value for the relief of cardiac pain of the diabetic Much harm has been done through the concept that insulin has a deleterious effect on the heart of the elderly diabetic it is the hypoglycaemic attack that is fraught with danger and this may be obviated with careful and proper use of insulin In their cases they protected the patient against even the mildest form of hypoglycaemic reaction Some of their patients have been free from attacks for as long as two years others have been greatly relieved and none of them was made worse by the use of insulin These results are attributed to careful protection of the patients against toxic insulin symptoms

Diabetic Coma —In a general article LAWRENCE (London) deals with the treatment of diabetic coma He remarks that in this era of insulin such a condition is rare and theoretically ought never to occur Impending coma should lead to diagnosis and treatment in

the early precomatose condition, thus allowing of its prevention by suitable treatment When full diabetic coma has developed through negligence or ignorance or from lack of prompt action, a fatal condition may develop, but coma as a cause of death ought to have disappeared by now Treatment consists in dealing with the ketosis by means of large doses of insulin with sugar to balance it, also correction of the dehydration and prevention of circulatory collapse by abundance of fluids

Three cases of sudden coma associated with disturbance in carbohydrate metabolism are reported by FLEMING, HERRING, and MORRIS (Glasgow), in none of these was the coma due to diabetes The association of coma with glycosuria almost inevitably leads to a diagnosis of diabetic coma In one case, although diabetic coma was first suspected, it became clear after further examination that the condition was due to pituitary tumour Typical acidotic breathing was absent The second case also appeared to be due to involvement of the pituitary The third case was almost certainly of nervous origin

BOWEN and associates (Buffalo) call attention to the similarity in symptoms between salicylate poisoning and diabetic acidosis, and to the possibility of their being confused They report the case of a child who showed the signs of diabetic coma, the urine reduced Benedict's solution, but also gave a strongly positive reaction with ferric chloride The spinal fluid also gave the violet colour characteristic of salicylate It was found that the child had had access to tablets containing acetylsalicylic acid and had swallowed several Salicylate poisoning should be considered when coma is present, especially if this is accompanied by hyperpnoea

Discussing the use of circulatory stimulants in diabetic coma, DODDS (London) says that in such cases the blood-pressure is usually low and the patient suffers from very depressed circulation, the force of cardiac contraction being poor In the terminal stages the pulse is imperceptible and the colour of the patient is bad A large intravenous dose of coramine (pyridine β carboxylic acid diethylamide) produces an immediate change The pulse becomes perceptible and the colour returns If the diabetic condition can be got in hand, such a patient will have a very much better chance than one whose circulation has not been stimulated Adrenaline and ephedrine appear to have little or no effect on this condition

Insulin Treatment —Dealing with the use and abuse of insulin, LAWRENCE (London) remarks that it should be used whenever the utilization of carbohydrate by the diabetic is insufficient to maintain the weight, health, and energy necessary for the demands of life, as shown by the persistence of glycosuria, ketonuria, and ill-health symptoms in diabetics on restricted diet It is essential in the treatment of coma and for the continuous welfare of most cases under forty, and in all children diabetics Many mild cases of

diabetes, mostly elderly, do not need it, but most would benefit and would be safer from complications with it It may be essential, too, to steer mild diabetics through temporary illness or operation, which makes diabetes worse Its chief use is, therefore, to metabolize an adequate diet for the patient's welfare by which he can and should be maintained in normal health, unless other complicating disease is present Unless insulin is producing this happy result it is at least being misused if not abused A serious abuse of insulin, now dying out, was to give short intensive courses for two to four weeks and then to stop it These cases, if at all severe, were rapidly improved in strength and weight, but deteriorated again almost as quickly when insulin was withheld Indeed, there was risk of coma when the treatment was interrupted

In a discussion on the physiological factors influencing the action of insulin, HIMSWORTH (London) refers to the dietetic factor Why does the giving of more carbohydrate result in apparent improvement in the patient's tolerance? Also why does the same measure result in an apparent increase in the ability of injected insulin to dispose of that carbohydrate? Recorded observations suggest that a correlation may exist between the effect of the diet on the sugar tolerance and its effect on the efficiency with which insulin acts in healthy man The dietetic factors which improve sugar tolerance also increase the sensitivity to insulin, while those which impair it decrease that sensitivity He concludes that the efficacy of insulin (natural or injected) is determined by the sensitivity of the body, which in turn is controlled by the carbohydrate content of the diet A type of diabetes exists which is due, not to lack of insulin, but to insensitivity of the body to its action this is the result of a lack of activating factor or possibly to the presence of an inhibiting factor

Among others taking part in this discussion, Marks suggests that the anterior pituitary may affect insulin response in two distinct ways it may accelerate recovery from insulin hypoglycaemia by facilitating the mobilization of liver glycogen, or it may exert a direct inhibitory effect upon the primary hypoglycaemic action of insulin Levy Simpson suggests that a release of adrenaline takes place during the hypoglycaemic state He believes that the normal level of blood sugar represents a balance between the antagonistic actions of endogenous insulin and endogenous adrenaline Many of the symptoms of hypoglycaemic shock are probably the result of a natural compensating hyperadrenalism and the injection of adrenaline in such a condition is illogical pituitary extract would be more suitable Goldblatt suggests that the thyroid maintains a state of tone in the sympathetic mechanism controlling glycogenolysis it keeps this mechanism in a condition of sensitivity to the action of adrenaline, thus allowing of an easily instituted recovery phase in the blood sugar curve after insulin

Protamine Insulinate—A development of insulin therapy, which holds out great promise, has been announced during the present

year For some time past efforts have been made to retard the absorption of insulin in order to spread its action over a longer period An oily suspension has been suggested, also injection along with a vasoconstrictor substance (see PRESCRIBER, 1935, Dec 373) Quite recently HAGEDORN and associates (Copenhagen) have succeeded in preparing a compound of insulin which is sparingly soluble in the tissue fluids This is protamine insulinate a combination of insulin with a mono-protamine obtained from the sperm of a species of trout *Salmo irideus* (The sperm of British Columbia river salmon is said to yield a suitable protamine) This is buffered with sodium phosphate and added to ordinary insulin, when a fine flocculent precipitate of highly insoluble protamine insulinate is formed The precipitate contains about one tenth of its weight of protamine The product is supplied in two phials—one containing 5 c cm of insulin Leo (40 units per c cm) and another containing 1 c cm of buffered protamine solution The latter is added to the insulin before use and the phial is well shaken The *pH* of this suspension approximates that of the plasma (7 3) When this suspension is injected considerable delay in absorption takes place and the fall in blood sugar is much more gradual and persists for a longer time

Clinical trials of protamine insulinate in fifteen cases of diabetes are reported by ROOT and associates (Boston) The results generally confirm the findings of the Danish workers the lowering action on the blood sugar being more even and more prolonged than that following ordinary insulin Certain inconveniences in its use are noted ordinary insulin is best for morning use and the new compound for the evening Further its use is contraindicated in coma where rapid action is essential

SPRAGUE and associates (Mayo Foundation) report on the clinical use of insulin protamine compound (insulin P) as compared with ordinary insulin When insulin P is used alone as a single dose before breakfast the meals of the first few days provoke glycosuria, but when the dose is properly adjusted the blood sugar level decreases progressively until after some days a normal level is attained The period of control may be shortened by supplementing insulin P for a few days with small doses of ordinary insulin the two should not be injected in the same site nor should they be mixed in the syringe Ordinary insulin is better when quick action is wanted as in acidosis The careless use of insulin P is attended with danger

The protamine compound has had considerable trial in this country LAWRENCE and ARCHER (London) confirm the findings of the Danish and American workers They conclude that it acts more slowly and for a longer period than ordinary insulin , that while it is weaker in dealing with ingested carbohydrate its action on endogenous sugar is equal to that of ordinary insulin It causes less symptoms of hypoglycaemia, but it is not strong enough in its action to control ingested carbohydrate Something combining the qualities of the two products would be more useful than either

BENNETT and GILL (London) have tested its effect on four severely diabetic children, all of whom had a tendency to hypoglycaemic attacks and persistent glycosuria in the morning. It was found that with protamine insulinate the total daily dose could be reduced, the patients were kept sugar-free, all severe reactions were abolished, and two doses daily were sufficient. At first there was a tendency to mild reactions during the night, but a slight adjustment of carbohydrate abolished this. The only difficulty encountered was in the measurement of the dosage.

Workers in Canada also have reported on its use. KERR, BEST, CAMPBELL, and FLETCHER (Toronto) have used it in twenty-five cases and find that the blood-sugar is not lowered so precipitately as with ordinary insulin; it slopes off more gradually and is less likely to pass below normal levels, rising slowly to previous levels. In severe cases and in juvenile and unstable diabetic patients, reactions due to hyperglycaemia are much less frequent. Protamine insulinate has presented new problems in the administration of insulin: adjustments of dosage and combined treatment with ordinary insulin are more effective in the control of some cases. Further experience is necessary before general rules for its use can be formulated.

RABINOWITCH, FOWLER, and CORCORAN (Montreal) record their experience in cases of severe diabetes. Their findings are very similar to those already mentioned. They observed that with use of ordinary insulin during the day and protamine insulinate during the night severe reactions occurred: these were avoided by the use of the protamine compound only. Protamine insulinate, they find, should not be used when quite fresh, as a certain amount of free insulin is present. After about five days it may be used, and it is then stable for months. (It is suggested by some workers that the new compound should be termed 'protamine insulin,' as the word 'insulinate' suggests chemical combination which has not yet been established.)

Crystalline Insulin.—Another form of insulin recently introduced is known as crystalline insulin. An insulin in crystalline form has been known for some time: this product is described as 'an improved crystalline insulin.' This substance is dissolved in dilute hydrochloric acid and the solution is adjusted to 40 units per c.cm. (B.P. insulin is 20 units per c cm.) with 0·1 per cent. tricresol as a preservative and 1·6 per cent. glycerol to render it isotonic. It is sterilized in the usual manner. It is similar to ordinary insulin in that it is stable and is dispensed as a single solution.

FREUND and ADLER (Detroit) report a comparison of this product with ordinary and protamine insulins as regards their effect on the blood-sugar level. Its action appears to be similar to that of protamine insulinate, but is more rapid in the onset of its action and shorter in the duration of its effect on the blood-sugar level.

MAINS and MCMULLEN (Chicago) report that crystalline insulin

is stable and is quite as potent as ordinary insulin. It shows slower absorption and more prolonged action. A single morning dose remains in effect during the succeeding night; one large daily dose may adequately control the blood-sugar of patients requiring two or more daily doses of ordinary insulin.

Protamine-Zinc-Insulin.—Since the introduction of the protamine compound, a number of substances have been found to act on insulin somewhat similarly, including several metals. Of these, zinc has been selected for trial, as it has been found to exist naturally in the pancreas, and to be a constituent of crystalline insulin (SCOTT and FISHER). To 500 units of protamine insulinate is added 1 mg. of zinc, the combination being made in acid solution. To this is added 1 c.cm. of buffer phosphate solution, which adjusts the reaction to that of the blood. Such a mixture is termed protamine-zinc-insulin. Like protamine insulinate it must stand for a few days to allow of the complete absorption of free insulin.

RABINOWITCH, FOSTER, FOWLER, and CORCORAN (Montreal) report trials with this compound. They find that the average requirement of protamine-zinc-insulin is about 25 per cent. less than during treatment with protamine insulinate. The addition of zinc apparently increases the sensitivity of the patient to insulin and less is required to produce the same effect. Protamine-zinc-insulin appears also to be effective in coma, which protamine insulinate is not. There was no evidence of toxicity due to the zinc.

Insulin Tannate.—GRAY (Santa Barbara, Calif.) reports trials with a compound of insulin and tannin. Addition of tannic acid to ordinary insulin produces a cloudy suspension of insulin tannate, which separates completely in twenty-four hours. Because of this instability the two solutions—insulin and tannic acid—are mixed in the syringe immediately before injection, the mixture containing 3 mg. of tannic acid per 100 units. This compound, he finds, has about 20 to 25 per cent. more hypoglycaemic action than ordinary insulin. Its relative insolubility delays absorption and allows of prolonged action. The hypoglycaemic effect is about equal to that of protamine insulinate.

Methods of Administration.—Discussing the time of administration, PLOTZ (Brooklyn) advises careful study of the insulin schedule in order to find each patient's individual requirements. This will necessitate its administration usually before but sometimes after meals or at odd times. This is all the more necessary with the newer and more slowly acting insulins. It should be given with regard to the actual food intake of the patient rather than in relation to a theoretical diet. Fractional examination of the urine is better than collection of 24-hour specimens. Divided doses are advocated by CLARK, GIBSON, and PAUL (Univ. of Iowa), who find that administration of small doses of equal unitage every two or four hours is more effective and requires less insulin than single large

doses, especially in the case of patients with acute infections or severe uncomplicated diabetes SINDONI (Philadelphia) is of opinion that administration should be fifteen or twenty minutes after, not before meals In this way the maximum effect is obtained when absorption of dextrose from the intestine is at its greatest and the tendency towards shock and hypoglycaemia is consequently less He has found this method work satisfactorily in practice

MAJOR (Kansas City) finds that insulin in ethylene glycol when dropped or sprayed into the nasal mucosa produces a definite and marked fall in blood-sugar both in animals and in diabetic patients The dose required by this route is considerably greater than that by subcutaneous injection, but the finding is of interest and may be of practical use in certain cases He used a solution of powdered insulin in ethylene glycol containing 500 units per c cm

Dietetic Treatment —ERCKLENTZ (Breslau) describes four cases in each of which the diet was chosen freely by the patient The condition of the first patient a man of 40 was unstabilized on 50 gm of carbohydrate with insulin ranging from 70 to 120 units He chose a diet of 2600 calories containing 390 gm of carbohydrate, 80 gm of protein and 121 gm of fat His insulin was increased from 120 to 150 units In the following days carbohydrate was increased to 494 gm and insulin was reduced to 130 units For ten days he took 473 to 500 gm of carbohydrate with 130 to 150 units of insulin He felt well had a good appetite, and put on weight His sugar excretion remained at from 6 to 11 gm per day At the end of the course carbohydrate had been gradually reduced to 150 gm and the patient was taking 130 to 150 units of insulin He had gained 14 4 kg (32½ lb) in weight and had become bright mentally and physically The other cases are also described in detail, and the method has been employed with success in over 100 cases Older diabetics require strict dieting but as a rule this routine was adopted Every patient on admission if not comatose received milk only for two days—one litre daily If the glycosuria disappeared and blood sugar was low, insulin was not given otherwise a mixed diet was given, and if sugar was excreted insulin was administered After some days the patient was allowed to choose his diet keeping to the same amounts of protein and fat but satisfying his craving for carbohydrate *With each increase of carbohydrate the dose of* insulin was adjusted After a while the craving for carbohydrate subsided and the patient voluntarily reduced the amount insulin being reduced accordingly The patient s condition was now regarded as stabilized and he was dismissed with full instructions for self treatment The mental effect of this treatment was remarkable, and it is suggested that actual regeneration of the islets took place, a suggestion supported by the absence of relapses in these patients

Miscellaneous Treatment —Prior to the advent of insulin many remed es were tried empirically and recommended for the



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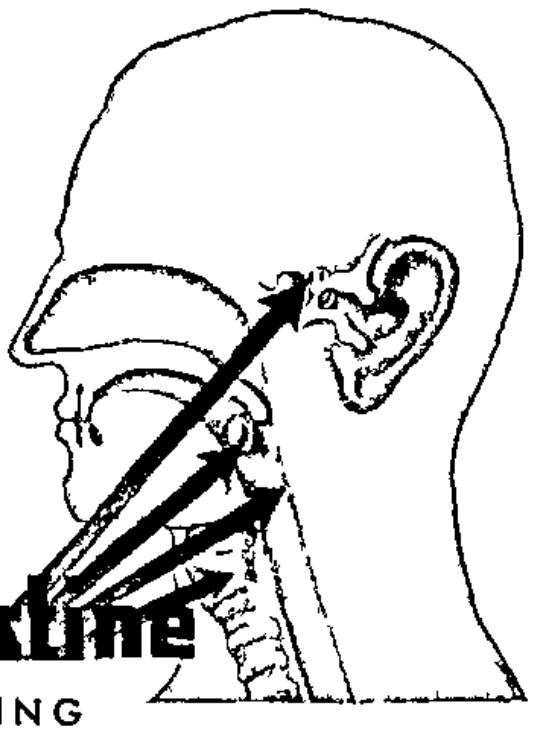
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treatment of diabetes Ever since insulin was introduced efforts have been made to find a substitute that could be given by the mouth With the exception perhaps of *Synthalin*, the guanidine derivative already described in these pages, none of these has found much favour

A new method of treatment has recently been reported from Russia SAKHAROV and ROSSIYSKIY (Moscow) describe an attempt to stimulate the pancreas by means of the serum of animals immunized by injection of human pancreatic tissue This serum contains a cytotoxin which has a specific action on the cells of the pancreas and is named *Pancreotoxin* It is given subcutaneously in daily doses of 0 1 to 0 2 c cm , a course consisting of 15 40 injections This method was tried in twenty five cases the patients' ages varying from 25 to 80 and the duration of the disease being from one to twelve years No insulin was given during or after this treatment, though some of the patients had been using it previously After from three to five injections of pancreotoxin the patients all showed an improvement in their general condition Glycosuria disappeared in some and was reduced in all, the blood sugar reverted to normal and the patients' tolerance to carbohydrate was raised Pancreotoxin, these workers conclude actually stimulates the life activity of the pancreas

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THERAPEUTIC NOTES.

Vincent's Infection: Acetarsone.—C. H. MAXWELL finds oral administration of acetarsone (stovarsol) gives better results than arsphenamine. The dose was 0·125 to 0·25 gm. three or four times daily, a paste containing acetarsone being applied locally at the same time.—*New York St. J. Med.*, June 1, '36, p. 874.

Tsetse Infection: Germanin.—H. L. DUKE (Uganda) reports that a dose of 2·0 gm. of germanin ('Bayer 205') administered to an adult will confer protection against *T. gambiense* and *T. rhodesiense* for three months or longer. In one case resistance lasted for 327 days after 1 gm. The more intense the exposure to infective tsetse the greater the benefit conferred by the drug.—*Lancet*, Feb. 29, '36, p. 463.

Arthritis: Vitamin D.—VRTIAK and LANG (Chicago) treated 20 cases of chronic atrophic arthritis with massive doses of vitamin D (irradiated ergosterol). Two showed marked improvement, ten moderate or slight improvement, eight no improvement. Nausea developed in all cases.—*J.A.M.A.*, Apr. 4, '36, p. 1162.

Toxic Effects of Carbarsone.—EPSTEIN (Los Angeles) records a case in which administration of carbarsone for dysentery was followed by acute fatty degeneration of the liver, exfoliative dermatitis, and death. Carbaminophenylarsonic acid is remarkably nontoxic and this is regarded as an exceptional case of intolerance.—*J.A.M.A.*, Mar. 7, '36, p. 769.

Jaundice and Phenobarbitone.—C. A. BIRCH (London) records the case of a man with well-marked hyperthyroidism who developed jaundice after one grain of phenobarbitone had been given daily for 22 days.—*Lancet*, Feb. 29, '36, p. 478. [In our issue of May last, p. 150, mention was made of antagonism between the thyroid hormone and barbiturates.—ED.]

Alcohol: Intraspinal Injection.—W. R. RUSSELL (Edinburgh) reports that intraspinal injection of alcohol often relieves the severe pain of malignant disease. He describes 18 cases so treated, and adds that the procedure is dangerous unless done with great care and strict attention to technique, as described in the article.—*Lancet*, Mar. 14, '36, pp. 595-599.

X-Ray Burns: Aloe Vera.—C. S. WRIGHT (Philadelphia) recommends application of the cut fresh leaf of *Aloe vera* Linn. (the plant yielding Socotrine aloes) as a remedy for early damage to the skin caused by x-rays. The fresh leaf is cut open and the thick latex applied to the burn, which healed rapidly in several cases described.—*J.A.M.A.*, Apr. 18, '36, p. 1363.

NEW REMEDIAL AGENTS.

New Drugs and Preparations.

[Under this heading are given brief notices of new non secret products as they appear on the market or are mentioned in medical literature The notes are intended for reference only, and must not be taken to imply anything in the nature of a recommendation In most cases the information is derived wholly or mainly from makers advertisements]

Acigen —A combination of mandelic acid sodium bicarbonate, ammonium biphosphate, and flavouring agents, in the form of granules, for oral administration in the treatment of urinary infections Dose, two teaspoonfuls (= 3 gm mandelic acid) in water four times daily after meals (Pharm. Specialities, May & Baker)

Colsulanyde —Sulphanilamide, a compound of the type of *p* aminobenzene sulphonamide, having a powerful action against streptococcal infections Indicated in meningitis, puerperal fever, erysipelas, septicaemia, and associated bronchopneumonia and otitis media Dose, 1 gm thrice daily after food, may be increased to 6 gm daily Issued as (*a*) suspension, 0 5 gm per teaspoonful, (*b*) powders, 7½ grains, (*c*) capsules, 0 25 gm (Crookes Labs)

Compound Halibut Oil Ointment.—A soothing, antiseptic, and antipruritic ointment containing 500 I U of vitamin A per gramme, and having the regenerative effect of this vitamin on the skin cells, also colloid kaolin and resorcin Recommended as a skin ointment of wide utility, applicable to wounds burns, bedsores, sunburn dermatitis, and other conditions (Crookes Labs)

Dmelcos —A stabilized emulsion of several strains of the Ducrey bacillus each c cm containing 250 million organisms Used for treatment of soft sores, chancres and buboes being said to heal rapidly under its influence A *Diagnostic Vaccine* is also supplied, which is double the strength, this was referred to in the note in our October issue, p 335 (Pharm Specialities, May & Baker, Ltd)

Endothyrin —A preparation of thyroid in two forms *Tablets*, each containing ½ grain of dry thyroid with an iodine content 2½ times that of the B P, with 5 grains calcium phosp co , *Guttae*, a liquid form of thyroid for oral administration, one drop being equivalent to 1 grain of fresh thyroid (about ½ grain dry thyroid), dose 1 to 10 drops (Endocrines-Spicer, Ltd)

Ergomonamine —The name suggested by Holden and Diver for a new alkaloid of ergot isolated by them. It has phenolic properties and does not give the characteristic colour reaction of the known ergot alkaloids —*Qtly J Pharm*, Apr -June 1936 p 230

Ferrous Chloride (Citrated) —A stable inorganic salt containing 68 per cent of ferrous iron in a form not readily oxidized Suitable for treatment of secondary anaemias Tablets, 3 grains each Dose, 3 to 6 tablets (9 to 18 grains) daily in severe hypochromic anaemia, in ordinary cases one or more tablets thrice daily (British Drug Houses)

Neo-Synephrin Hydrochloride.—The laevorotatory isomer of synephrin, a synthetic substitute for ephedrine (see PRESCR., 1931, Feb., 73). More powerful than synephrin as a vasoconstrictor and less toxic than ephedrine. Applied locally as 0·25 to 1 per cent. solution; used also as an addition to local analgesic solutions instead of adrenaline.—*J. Amer. Dent. Assoc.*, Oct. '36, p. 1974.

Panopsin.—Pancreatic amylopsin, prepared from the acinous cells of the pancreas, together with such trypsin as may be retained. Will convert 500 times its weight of starch into sugar and digest 90 times its weight of casein. Indicated in defective digestion and in all conditions of malnutrition. Tablets, 2½ grains. Dose, one or two tablets just before meals (Endocrines-Spicer).

Perandren.—The propionic acid ester of testosterone, the synthetic male hormone described in our issue of May last (p. 204). Its use is suggested in testicular insufficiency (male climacteric), sexual maldevelopment, eunochoidism, and prostatic affections. In oily solution, 5 mg. per c cm. (250 international units). Dose, 1 c.cm. once or twice a week, intramuscularly or subcutaneously (Ciba Ltd.).

Prontosil Album Tablets.—A non-staining form of prontosil (see PRESCRIBER, Sept. 1936, p. 292) for oral administration in streptococcal infections. Tablets, 5 grains. Dose, one or two tablets daily, alone or in conjunction with intramuscular injections of prontosil soluble (Bayer Products).

Rheumotropin.—A combination of phenylcinchoninic acid (cinchophen) with hexamine and quinine in the form of tablets (0.5 gm. each) for treatment of rheumatic affections. Dose, 1 to 2 tablets, 3 or 4 times daily (Silten Ltd.).

Ryzamin-B.—The concentrated and purified vitamin B fraction of rice polishings: potency 50 I.U. vitamin B per gm. Allows of addition to the diet of an adequate supply of the antineuritic factor. Dose, 0·4 gm. daily as dietary supplement; in serious cases (beri-beri and late sprue) up to 4 gm. or more daily. A golden-brown syrupy product, issued in collapsible tubes with measuring spoon (Burroughs Wellcome).

Scuroform Anaesthetic Lozenges.—*Contain each 2 mg. scuroform* (butoform: see PRESCRIBER, Apr. '36, p. 130) Act as local anaesthetic, giving relief in painful conditions of mouth and throat, cough, etc. (May & Baker).

Tannocarbon.—Tablets containing medicinal charcoal 0·13 gm. and tannin albuminate 0·13 gm. in each. Indicated in acute infectious intestinal diseases and in fungus poisoning. Dose, 2 to 6 tablets (Gedeon Richter).

Thiarsin.—An organic compound of arsenic containing 20 p.c. of As and equivalent to sulpharsphenamine, B.P. (Bengal Chem. and Pharm. Works, Calcutta).

REVIEWS OF BOOKS.

Vascular Disorders of the Limbs By Sir Thomas Lewis, *C.B.E.*, F.R.S., M.D., etc. Pp. 111. (Macmillan. 6s. 6d.)

There are some conditions which on a superficial view are apparently capable of easy explanation, and only when subjected to a careful and instructed critical review do their essential difficulties reveal themselves. Among such are certain peripheral vascular disorders, the anatomy and physiology of which Sir Thomas has set himself to unravel. Some excellent work was done many years ago in Dorpat, but the subject has probably never been so fully expounded as is now done by Sir Thomas Lewis. The points he brings out can be made the subject of test by any clinician: he puts commonly observed facts, hitherto explained on rather slender evidence, on a sound physiological footing. The study will well repay careful and repeated reading. J. O.

Appendicitis: When and How to Operate By W. J. Stewart McKay, M.B., M.Ch. Pp. 260. (Angus & Robertson, Sydney. 12s. 6d.)

Written as a guide to the general practitioner, this addition to an already extensive literature on the subject strikes rather a new note. The whole outlook is simple and clinical, and the author maintains throughout a simplicity of diction and argument that enables him to carry his reader step by step from the simple to the complicated case. One feels that he has succeeded in instructing the general practitioner, say in the country, who aspires to carry out by himself the necessary surgical measures in his cases. At the same time there is a great deal of useful practical teaching in the various chapters on diagnosis, prognosis, and treatment. Quite an interesting and useful book. J. O.

Clinical Handbook for Residents, Nurses and Students By Members of the Staff of St. Vincent's Hospital, Sydney. Edited by Victor M. Coppleson, F.R.C.S., and Douglas Miller, F.R.C.S. Pp. 205. (Angus & Robertson, Sydney. 6s.)

A careful perusal of this volume satisfies one that residents, students, and nurses have at their disposal an excellent practical guide to ward work. Practically all the procedures included among the duties of residents and nurses are dealt with in clear unambiguous language, with sufficient detail and without redundancy. Minor surgical procedures, preparation for x-ray work, clinical pathology, anaesthesia, blood transfusion, and dietetics all find appropriate mention, while some points are included dealing with general nursing and that necessary in ophthalmic, skin, ear, nose and throat, and gynaecological cases. This excellent and well arranged volume would be very good value even at a higher price than six shillings. J. O.

Absorption from the Intestine By F. Verzár, Professor of Physiology, University of Basle, assisted by E. J. McDougall, Ph.D. Pp. 294. (Longmans, Green. 21s.)

The series of Monographs on Physiology is well known, and this volume is one which gives an ample review of the whole subject with a

voluminous bibliography From the facts now known regarding the absorption of water and salines, the reader is taken through the absorption of metals, proteins, carbohydrates, fats, gases, etc., with full historical and experimental detail and with such clarity that the reader can readily grasp all the points as they are successively presented This is an excellent and authoritative manual for reference J O

Bainbridge and Menzies' Essentials of Physiology Eighth Edition Edited by H Hartridge, M D , Sc D , F R.S Pp 651 (Longmans, Green 14s)

The seventh edition of this book appeared four years ago, and since then advances in knowledge have been considerable, necessitating numerous changes and additions New chapters have been added dealing with the nutrition of the heart, the oxygen carrying power of the blood, the vitamins, tissue oxidation, synapses, and pregnancy and parturition, while almost all the older chapters have been revised and augmented This edition is some seventy pages larger than the last, but it is still of convenient size The matter is arranged in short paragraphs, simple and lucid in their wording and each headed in bold type , this makes for easy reading and ready mastery of the subject, while the illustrations are clear and helpful This edition well maintains the position held by the book for over twenty years as a standard textbook it gives the ' essentials ' without unnecessary detail, and will be of great value not only to students but to those who wish to keep their knowledge to date T S

The Essentials of Chemical Physiology By the late W D Halliburton, J A Hewitt, Ph D , D Sc , and W Robson, Ph D , D Sc Thirteenth Edition Pp 350 (Longmans, Green 9s)

Since the appearance of the twelfth edition of this book, its originator, Professor Halliburton, has passed away, and the authorship now rests with those who were his colleagues The book is no longer divided into elementary and advanced sections these are now fused and the result is that this book is smaller by some thirty pages Deletion of the section on organic chemistry, now a separate subject, has allowed of the introduction of certain new matter, and the work may now be regarded as thoroughly up to date This is important, as the advances in chemical physiology since 1929, when the last edition appeared, have been considerable In all respects the essential character of the book remains unaltered and it maintains its reputation as a standard textbook T S

Materia Medica for Dentists By Frank Coleman, L R C P , M R.C S , L D S Seventh Edition Pp 352 (Milford 10s 6d)

Since the last edition of this book appeared the British Pharmacopoeia, 1932, has been issued and numerous changes have been made necessary These have been faithfully carried out, and as the additions and deletions almost balance each other the book remains about the same size Among the additions may be noted snake venom as a haemostatic, evipan sodium as an intravenous anaesthetic, and other drugs of special interest to dental surgeons The Pharmacy and Poisons Act and the Dangerous Drugs Acts are fully explained The book has been brought thoroughly to date in other respects and is admirably suited to the requirements of dental students and practitioners

Favourite Prescriptions Edited by Sir Humphry Rolleston, Bart, and Alan A Moncrieff, M D Pp 227 (Eyre & Spottiswoode 10s 6d)

This book consists of a series of articles on the Hospital Pharmacopoeias by various writers, these appeared in *The Practitioner* and are now reprinted in book form Altogether eighteen of these works are described, the principal formulae in each being cited and a running commentary supplied by the author Hospital formulae may be regarded as tried prescriptions evaluated by experience, indeed some of those appearing in this book are linked with the names of famous physicians A selection from the National Formulary (Health Insurance) concludes the series and an index enables the reader to find any particular formula with ease The book should prove useful to practitioners

The Masseur's Companion By Arthur J Bowman, M I C M, B P A, M B A Ch Pp 100 text, 100 notes (Actinic Press Paper, 4s, leather cloth, 5s)

This little pocket book puts forward no claim to be a textbook, but is offered to masseurs as a book of reference of a handy size suitable for *carrying about A brief synopsis is given of each condition that may* have massage as part of its treatment, followed by instructions regarding the proper type of physiotherapy The book is interleaved with blank pages on which the practitioner can write his own additional notes Instructions are of necessity somewhat brief as regards the methods of treatment other than massage, but the descriptions pertaining to the speciality are well tabulated, easily and quickly digested, and well chosen It would have been better had the book been read by a medical consultant before it was printed, as there are several errors both of description and of technique No mention is made, for example, of the usual cause of torticollis, and one doubts the wisdom of local effleurage to an appendix scar eight days after operation Nevertheless it is a useful book and well serves its purpose W M

MEDICAL RESEARCH COUNCIL SPECIAL REPORTS

No 213 *The Nutritive Value of Fruits, Vegetables and Nuts* By R A McCance, E M Widdowson, and L R B Shackleton (H M Stationery Office 2s)

This is a further report on the important subject of nutrition It deals with the chemical composition of fruits, vegetables, and nuts, and the changes in their constituents brought about by cooking It is shown that chemical analysis of a food may be misleading as a guide to its nutritional value, because some of the material estimated may not be available for nutrition. Further, the presence or absence of one constituent in a food may influence the availability of others This report deals with the subject very thoroughly and contains much useful information

No 215 *Artificial Pneumothorax Experience of the London County Council* By T J Bentley, M D, M R C P, D P H (H M Stationery Office 1s 6d)

The extensive employment during recent years of artificial pneumothorax in the treatment of pulmonary tuberculosis has rendered desirable

the publication of this report. A review is given of the literature of the subject since 1922, and the fate of patients receiving this treatment under the scheme of the London County Council during ten years is analysed. Artificial pneumothorax is found to have a limited application, only about ten per cent. of the patients undergoing residential treatment being regarded as suitable to receive it. In properly selected cases, however, it is shown to be of vital importance, increasing the patient's working capacity and expectation of life. It is also suggested that the method may be more widely applied, especially in earlier cases and in young male adults.

No. 216. Medical Uses of Radium. (H.M. Stationery Office. 1s)

The researches on radium therapy during 1935, as carried out in various centres throughout the country with radium and radium emanation distributed by the Council, are summarized in this report. The accounts given in thirteen previous reports are thus continued, and the progress of radium treatment is reviewed to date.

No. 217. The Relationship of the Iodine Contents of Water, Milk and Pasture to the Occurrence of Endemic Goitre in Two Districts of England. By M. Young, M. G. Crabtree, and E. M. Mason. (H.M. Stationery Office. 6d.)

The investigation described in this report was undertaken by the Committee on Iodine Deficiency and Thyroid Disease and follows on previous reports on the subject. A remarkable difference is shown in the incidence of thyroid enlargement in children in different counties in England: in Suffolk this is only 3 per cent., while in Somerset it rises to 56 per cent. This high incidence is associated with a low iodine content of the local water, but it is shown further that other factors contribute to the high incidence and complicate the situation. The report indicates the lines upon which further investigations may profitably be made.

The Home Office has issued a MEMORANDUM ON THE PROVISIONS OF THE PHARMACY AND POISONS ACT, 1933, as it affects medical, dental, and veterinary practitioners, hospitals, dispensaries, etc. (H.M. Stationery Office, 3d.). It shows the main requirements of this rather detailed Act, how poisons are to be obtained, how prescribed, how dispensed, how stored, and concludes with a list of poisons and their relation to the first schedule. It does not deal with the requirements of the Dangerous Drugs Acts applying to those poisons which are also Dangerous Drugs.

The Industrial Labour Office, Geneva, has issued a book of 330 pages entitled INDUSTRIAL ENVIRONMENT AND HEALTH (7s 6d.), a compendium designed to give authoritative information to lay persons who have to do with supervision of hygiene in factories, etc. While the information will enable such persons to employ the necessary measures intelligently it is not suggested that they can themselves carry them out in all the practical details. In eight chapters, each written by an expert, such subjects are dealt with as atmospheric pressure, temperature, humidity, estimation of noise, etc, all of which are so full of detail that one sometimes wonders whether they are not beyond the layman's capacity.

The 67th Annual Report of the NATIONAL INSTITUTE FOR THE BLIND shows that more blind students are now undergoing training than at any time since the School was opened twenty-one years ago Eighteen men and seven women are taking courses in massage, remedial exercises, and electrotherapy, and during the year ten blind students successfully passed the examinations of the Chartered Society of Massage and Medical Gymnastics At the Clinic attached to the School over 5000 attendances were recorded and nearly 8000 treatments were given, all being carried out by senior students under supervision The report is most interesting and well shows the good work this Institute is doing

THE ANGLO-YUGOSLAV REVIEW is a quarterly publication issued by the Society for Promoting Anglo-Saxon Culture in Yugoslavia, Belgrade It contains articles in English dealing with various aspects of life and work in Yugoslavia and is designed to promote friendly relations with this country The address of the publishers is Jakšiceva, 2, Belgrade, and the price is 2s 6d a copy

The Cumberland Development Council Ltd, 30 Roper Street, Whitehaven, has issued a beautifully illustrated brochure entitled WONDERFUL WEST CUMBERLAND (2s 6d) This is designed not only to attract visitors—which it certainly ought to do—but also to promote the establishment of industries in West Cumberland, which is one of the 'depressed areas' though one would not think so from the pictures It is to be hoped that this well produced brochure will have the desired effect

CHRISTMAS SEALS—The sale of Christmas Seals which was introduced into this country in 1933 under the auspices of the National Association for the Prevention of Tuberculosis is now in its fourth season The seals, which cost only ½d each are attached to letters and parcels, particularly at Christmas time, a practice which not only renders valuable financial assistance to the various organizations dealing with the care of tuberculosis, but also serves as an excellent method of propaganda by drawing attention to the need for universal co-operation in fighting this disease In Scotland the sale is under the direction of the Royal Victoria Hospital Tuberculosis Trust at 65 Castle Street, Edinburgh, 2

Messrs William R Warner & Co Ltd have issued their annual CALENDAR OF MEDICAL HISTORY for 1937 As in former years this consists of a diary giving a page to each day, with useful or interesting notes at the foot of each page At the end of the book is an amount of statistical information for ready reference The text is well printed, the paper has a good surface for writing and the book is dauntily bound in blue leather cloth Distribution is to the medical profession only, and is restricted to those in Great Britain, and copies will be sent out early in December The firm's present address is 300 Gray's Inn Road, London, W C 1, but after January 1, 1937, it will be Power Road Chiswick, W 4

Messrs Boots Pure Drug Co Ltd have published a new edition of their booklet INSULIN BOOTS IN THE TREATMENT OF DIABETES MELLITUS revised and brought to date It deals with the history and properties of insulin and with the diagnosis and treatment of diabetes, and it contains the 'line ration' diet scheme and details of the various urine tests A copy will be sent to any reader of THE PRESCRIBER on application to the Company's Wholesale Department, Station Street, Nottingham

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'I offer my hearty congratulations on the completion of thirty most useful years of existence, and I trust that the work will continue to be of the high standard hitherto maintained by your good self'—G ARBOUR STEPHENS, M D, Swansea

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'I should like to prescribe continued success for your work and all happiness to yourself'—W T P, Newcastle-upon-Tyne

'Congratulations upon the completion this month of thirty years of successful editing and publishing of THE PRESCRIBER. More power to you'—C R P, Chicago, U S A.

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